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CHEMOTHERAPY OF MALIGNANT NEOPLASTIC DISEASES

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Chemotherapy of cancer has been studied intensively in recent years. Attempts to inhibit tumor growth by means of drugs have been made since ancient times, but not until the last decade have potent carcinolytic compounds been discovered which can be tolerated by animals and human beings in at least partially effective doses. The enormous literature which has now accumulated on this subject has been summarized in several recent reviews.[1] Drugs which have aroused a great deal of interest include Serratia marcescens (Bacillus prodigiosus) polysaccharide, KR (carcinolytic substance of Trypanosoma cruzi, named after Klyueva and Roskin), antireticular cytotoxic serum (ACS), stilbamidine (4,4′-stilbenedicarboxamidine) and ethylstibamine (neostibosan®), folic acid conjugates, folic acid antagonists, urethane and the nitrogen mustards (2-chloroethyl amines). The data available at present indicate that all but the last three of these substances are either biologically inactive or are too toxic to be practical for clinical application. Neither the radioactive isotopes nor endocrine substances used in therapy of cancer will be discussed in this paper, as it is considered that they do not fall within the scope of the term chemotherapy.

At present, chemotherapy of cancer is at best palliative and retardation of tumor growth, when it occurs at all, is temporary. The intense research activity in this field is apparently based on the assumption that it is theoretically possible to destroy completely or prevent the multiplication of malignant cells by the administration of drugs without irreparably damaging normal cells. However, some of the most experienced investigators in the field of cancer research doubt whether cure of cancer in this sense is within the realm of possibility,[2] and certainly this goal is not apt to be achieved within the near future.

STILBAMIDINE AND ETHYLSTIBAMINE

Stilbamidine is known to be effective in the treatment of kala-azar. As both kala-azar and multiple myeloma are characterized by hyperglobulinemia, Snapper[22] began treating multiple myeloma with this drug. The rationale for this use of stilbamidine is not clear, as the drug acts directly on the parasite causing kala-azar and has no effect on the abnormal protein; furthermore, the abnormal protein in kala-azar is not the same as the abnormal protein in myeloma.[22] Nevertheless, Snapper observed that, after administration of the drug, large basophilic inclusion bodies appear in the myeloma cells but not in any other cells in the bone marrow, and these bodies have been shown to contain large amounts of ribose nucleic acid.[24] The suggestion is made that stilbamidine may specifically dissociate the nucleoproteins of myeloma cells. Snapper reported that concomitant with the appearance of the granules clinical improvement frequently occurred, and the drug seemed to have a specific influence on the severe bone pain of this disease. Bone pain improved in 80 per cent of the cases.

Karnofsky[16] quoted an analysis by Gibson and Pogge of a pooled survey of 186 patients with multiple myeloma treated with this drug: 24.7 per cent experienced complete relief of pain, and 38.7 per cent obtained partial relief of pain; the remainder of the patients were unimproved or became worse. In 79 of 99 cases studied by serial roentgenologic examination there was no increase in the size of the lesion, but lesions seldom decreased in size. Facial neuropathy had developed in 30 of the patients.

Five patients with multiple myeloma have been treated with stilbamidine by us. Inclusion bodies as described by Snapper appeared in the myeloma cells, and 2 of the 3 patients who complained of pain experienced partial relief. The other 2 patients had severe anemia and thrombopenia but no pain; neither of these patients showed improvement.

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The sections of the original paper on Products of Bacteria and Proteins (toxins derived from streptococci and Serratia marcescens, purified S. marcescens polysaccharide and KR vaccine) and Tissue Extracts and Tissue Products (particularly antireticular cytotoxic serum) have been omitted from THE JOURNAL because of lack of space, but they are included in the authors' reprints, which are available on request.

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2. (a) Waghen, W. H.: General Review of Cancer Chemotherapy, in Approaches to Tumor Chemotherapy," pp. 1-12. (b) Haddow, A.: Note on Chemotherapy of Cancer, Brit. M. Bull. 4:417, 1947.

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Rubenstein [25] treated patients having multiple myeloma with ethylstibamine, an antimony compound which is also effective against kala-azar, and observed relief of bone pain and basophilic granulation of the tumor cells.

In summary, the evidence at present is not convincing that either stilbamidine or ethylstibamine is of great value in the treatment of multiple myeloma. Although relief of bone pain sometimes occurs, there is no evidence that multiplication of the tumor cells is significantly retarded or that the duration of the disease is increased.

URETHANE

In 1946 Haddow and Sexton [26] published the results of their studies on the effect of carbamic esters (urethanes) on spontaneous mammary adenocarcinoma in mice and the Walker rat carcinoma. Urethane was found to retard the growth of these tumors. Patterson and her associates [27] then treated far advanced cases of malignant disease in humans with unimpressive results, but it was noted that leukopenia frequently developed; this observation led to the trial of urethane in human leukemia. The results were encouraging, and many reports [28] have appeared since then on the effects of urethane on animal and human leukemia.

Gellhorn and Jones [15] have recently summarized data from the literature on 108 patients with leukemia treated with urethane: in 40 patients with acute leukemia urethane therapy was without benefit; in 46 patients with chronic myelocytic leukemia the immediate response was satisfactory in 30 (65 per cent); 11 of 29 patients with chronic lymphocytic leukemia (38 per cent) responded satisfactorily.

The recommended dosage of urethane is 2 to 5 Gm. daily for two to six weeks or until the leukocyte count drops to 20,000. Toxic manifestations (of urethane therapy) include nausea, vomiting and severe depression of bone marrow activity.[29] Six patients with chronic myelocytic leukemia have been treated with urethane at the Washington University Medical School; in 2 of these patients severe thrombopenia developed. In at least 1 of these patients the thrombopenia could probably be attributed to the drug.

A man aged 54 has had chronic myelocytic leukemia since about March 1948. On Feb. 9, 1949, when urethane therapy was started, he had had no therapy of any sort for seven months; he was asymptomatic, and the only abnormal physical signs were slight enlargement of the axillary lymph nodes and splenomegaly. Examination of his blood at that time showed 5,160,000 erythrocytes, 14.1 Gm. hemoglobin, 76,000 leukocytes, 720,000 thrombocytes and 2.8 per cent reticulocytes, with a differential count of 50 segmented neutrophils, 13 stab cells, 2 eosinophils, 7 metamyelocytes, 15 myelocytes, 8 lymphocytes and 4 monocytes. The patient received 2 Gm. of urethane daily from Feb. 9 until March 23, 1949, at which time his thrombocyte count was 83,000. The dosage of urethane was then decreased to 1 Gm. daily until April 11, when it was discontinued because of profuse epistaxis and innumerable petechiae; practically no thrombocytes could be found in the blood. The leukocyte count decreased to 1,000 per cubic millimeter. The thrombocyte level remained less than 10,000 per cubic millimeter until April 30, when it began to rise slowly; by May 26, 1949 the thrombocyte level was 70,000 and all bleeding had stopped. On June 3, 1949 the thrombocyte count was 348,000.

It is not possible at the present time to evaluate the relative merits of urethane compared to roentgen ray, P^{32} and nitrogen mustard in the treatment of chronic leukemia, but the data in the literature and our own limited experience do not suggest that urethane will supplant these other forms of therapy.

Urethane has also been reported to be effective in metastatic prostatic carcinoma [30] and multiple myeloma.[31] Three patients with multiple myeloma have been treated with urethane at the Washington University Medical School. One was definitely relieved of severe bone pain; the other 2 patients showed no clear-cut benefit, but they were unable to tolerate recommended doses of the drug because of nausea.

VITAMINS AND VITAMIN DEFICIENCIES

The effect of vitamins and of vitamin deficiencies on tumor growth has been studied. Attempts to retard tumor growth by the production of biotin deficiency have been unsuccessful.[32] Production of a pyridoxine deficiency apparently inhibits the growth of certain transplanted tumors in mice [33] but there is no evidence that this is a specific effect.

Teropterin [9] (pteroyltriglutamic acid—a folic acid conjugate), in a series of 90 patients with a variety of malignant tumors, has been reported to improve the sense of well-being, the appetite and strength of the patients and to relieve pain.[34] The use of teropterin [9] in the treatment of malignant neoplastic disease stems from the reports of Lewisohn and others [35] that yeast extract, pearled barley extract and Lactobacillus casei factor (folic acid) caused regression of sarcoma 180 in mice in a significant percentage of animals. Sugiura,[36] Zahl and Hunter [37] were unable to confirm this work.

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37. Zahl, P. A., and Hunter, S. H.: Note: Growth Inhibition of Mouse Sarcoma 180, in Approaches to Tumor Chemotherapy,[36] pp. 214-216.

The Council on Pharmacy and Chemistry of the American Medical Association analyzed reports which it received on teropterin[9] and diopterin[9] (pteroyldiglutamic acid) therapy of 275 patients and concluded that there is no convincing evidence that these substances produce significant objective improvement in any type of cancer.[38] On the basis of our experience with teropterin,[9] we wholeheartedly agree with Karnofsky's [10] recent statement that "the therapeutic effects ascribed to teropterin[9] are couched in such tenuous and devious terms that they defy critical analysis. In the absence of reproducible and consistent objective evidence of effect on neoplastic disease, teropterin[9] cannot be regarded seriously as a chemotherapeutic agent against cancer."

FOLIC ACID ANTAGONISTS

The treatment of acute leukemia with folic acid antagonists has aroused tremendous interest. Several years ago Farber,[39] Heinle [40] and Bethel [41] observed that the administration of folic acid or its conjugates apparently intensified the severity of acute leukemia. It was natural, therefore, that when synthetic compounds which antagonize the physiologic activity of folic acid were prepared [42] their effect on acute leukemia should be studied.

The folic acid antagonists have been tested on chicks,[42] swine,[44] rats [43a] and mice.[43b] A detailed study of the hematologic changes induced in guinea pigs by the prolonged administration of folic acid antagonists is now in press.[45] Different species of animals show striking differences in susceptibility to the effects of aminopterin (4-amino pteroylglutamic acid).[46] When relatively large doses are given, furthermore, their effects can be prevented only in part, if at all, by extremely large amounts of folic acid or liver extract, either singly or in combination.[47]

Farber and associates [48] initially reported observations on 16 children with acute leukemia treated with aminopterin (4-amino pteroyl-glutamic acid). Ten of these children showed temporary clinical and hematologic improvement. In a later report Farber [49] summarized data on 60 children with acute leukemia treated for three weeks or longer with aminopterin, amethopterin (4-amino-methyl-pteroylglutamic acid) or amino-an-fol (4-aminopteroylaspartic acid). Definite clinical and hematologic improvement occurred in "somewhat more than 50 per cent" of these patients. At the time of this second report 1 child was still alive twenty-three months after the onset of his disease, and the leukemia in another was under control sixteen months after onset. According to Farber,[49] Diamond observed spontaneous remissions in 10 per cent of 300 children with acute leukemia, the remissions averaging less than ten weeks in duration. The incidence of spontaneous remissions at the St. Louis Children's Hospital is less than 1 per cent.[50] Consequently, the results obtained with folic acid antagonists cannot be attributed to spontaneous remissions.

Farber [49] has also reported inconstant but definite temporary carcinolytic effects of these folic acid antagonists on other forms of cancer, including neuroblastoma, pulmonary metastases from cancer of the bladder, lymphosarcoma and Hodgkin's disease.

We have treated 17 patients having acute leukemia with aminopterin or amino-an-fol; significant remissions occurred in 6 instances. Data on one of these patients are presented:

History and Examination.—W. M., a man aged 49, noted the onset of pallor and weakness about Dec. 1, 1948. About Jan. 15, 1949 he was found to be anemic, and three blood transfusions were given with temporary improvement. On February 11 fever, nasal congestion and a slight sore throat developed. Fever persisted, and the patient began to have occasional chills. A cough developed. He was given two more transfusions. Physical examination on March 1 revealed that the temperature was 40 C. (104 F.), the pulse rate 120, and the patient showed decided pallor. Scattered flame-shaped hemorrhages were present in both fundi. Lymph nodes were not enlarged, and the liver and spleen were not palpable. The leukocyte count was 600 per cubic millimeter; erythrocytes numbered 1,860,000; the hemoglobin content was 6 Gm. per hundred cubic centimeters; thrombocytes, 650,000, and reticulocytes, 0.1 per cent, with a differential count of 98 per cent leukemic lymphocytes, 1 per cent stab cells and 1 per cent monocytes. The sternal bone marrow contained 99 per cent leukemic lymphocytes, and only 1 nucleated red cell was seen per 100 leukocytes. The diagnosis was acute lymphocytic leukemia (leukosarcoma), subleukemic variety.

Treatment and Course.—Therapy and the hematologic response thereto are charted in figure 1. The patient was given penicillin, streptomycin and blood transfusions. Administration of amino-an-fol, 40 mg. intramuscularly daily, was started on March 3, and the dosage was later decreased as shown. Within five days after amino-an-fol therapy was started the temperature of the patient began to fall, cough subsided and strength began to improve. By the twelfth day of therapy he was asymptomatic except for moderate weakness, and blood cell counts were: 7,100 leukocytes; 2,770,000 erythrocytes; 8.4 Gm. hemoglobin per hundred cubic centimeters; 238,000 thrombocytes, and 0.1 per cent reticulocytes with a differential count of 67 per cent segmented neutrophils, 4 per cent stabs, 1 per cent metamyelocytes, 2 per cent C myelocytes, 25 per cent small mature lymphocytes and 1 per cent monocytes. Sternal bone marrow examination was repeated on the fifteenth day of therapy; 65 per cent of the cells in the marrow were leukemic lymphocytes, and less than 1 nucleated red blood cell was seen per 100 leukocytes. The patient was asymptomatic

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47. Innes, Innes and Moore.[45] Minnich and Moore.[46]

48. Farber, S.; Diamond, L. K.; Mercer, R. D.; Sylvester, R. F., and Wolff, J. A.: Temporary Remissions in Acute Leukemia in Children Produced by Folic Acid Antagonist, 4-Amino-pteroyl-Glutamic Acid, New England J. Med. 238:787, 1948.

49. Farber, S.: Some Observations on the Effect of Folic Acid Antagonists on Acute Leukemia and Other Forms of Incurable Cancer, Blood 4:160, 1949.

50. Cooke, J. V.: Personal communication to the authors.

at this time except for mild weakness. His strength never returned to normal, but he had no other symptoms until about May 1, 1949, when there developed malaise, anorexia and vague indigestion. On May 10 the blood cell counts were: 5,900 leukocytes; 2,590,000 erythrocytes; 9.2 Gm. hemoglobin per hundred cubic centimeters; 41,000 thrombocytes, and no reticulocytes, with a differential of 47 per cent segmented neutrophils, 4 per cent stab cells, 2 per cent metamyelocytes, 6 per cent myelocytes, 21 per cent small mature lymphocytes, 14 per cent leukemic lymphocytes and 5 per cent monocytes. A bone marrow examination on the same day revealed 83 per cent leukemic cells. The dosage of amino-an-fol was increased to 40 mg. daily; by May 16 the patient felt better and the dosage was

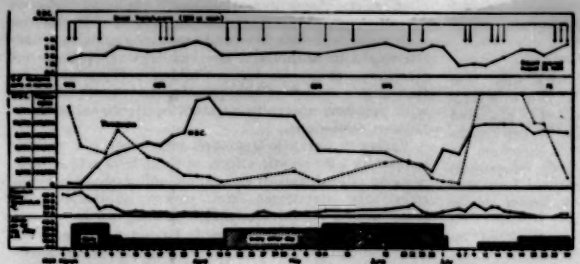

Fig. 1.—Therapeutic data and hematologic response to Amino-an-fol of W. M., a man aged 49 with acute lymphatic leukemia (leukosarcoma).

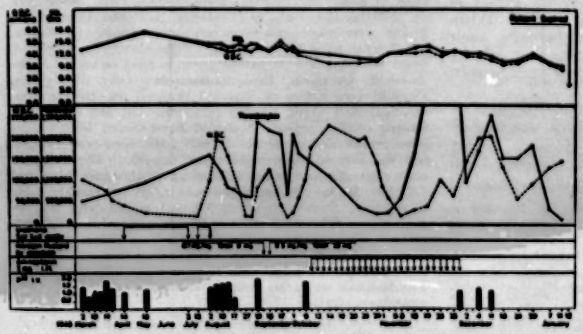

Fig. 2.—Therapeutic data and hematologic response of L. R., a man aged 34, with chronic myelocytic leukemia treated with P^{32}, urethane, nitrogen mustard and aminopterin.

decreased to 40 mg. every other day. He felt fairly well until about June 6, when weakness and anorexia became worse and an ulcer on his hip and mild epistaxis developed. Blood cell counts on June 13 showed 5,800 leukocytes per cubic millimeter, only 1 per cent leukemic lymphocytes in the blood differential, and 39 per cent leukemic lymphocytes in the bone marrow. The dosage of amino-an-fol was increased to 40 mg. daily. On June 21 he was readmitted to the hospital with jaundice and hemorrhagic lesions of the gums and pharynx. Bilateral pulmonary mottling, which was interpreted as leukemic infiltration, was noted on roentgen examination of the chest. The icterus index was 38; the sodium bilirubin level was 4.1 mg. and bilirubin globin 3 mg., per hundred cubic centimeters; urobilinogen was present in the urine up to a dilution of 1:80, quantitative urobilinogen measured 0.39 Ehrlich units per two hour (afternoon) specimen; a cephalin-cholesterol flocculation test was negative on June 24 and again on July 7. Intensive amino-an-fol therapy was continued until July 2, when this treatment was stopped because of increasing severity of the hemorrhagic, necrotic gum and pharyngeal lesions. Within ten days the patient's gums improved considerably, and amino-an-fol therapy was resumed (10 mg. daily). By July 15 the gums had cleared up entirely, the temperature was normal, and the jaundice had decreased. Bone marrow examination on July 27 showed only 7 per cent leukemic lymphocytes. A roentgenogram of the chest on July 29 showed entirely clear pulmonary fields. The patient was discharged from the hospital July 31, feeling well except for continued weakness. He continued to take amino-an-fol, 15 mg. daily, at home. He died at his home in another city Aug. 22, 1949.

Necropsy Data.—A postmortem examination was performed at St. Mary's Hospital, Jefferson City, Mo., and we were able to obtain the paraffin blocks of the tissues from that institution. The following report made from the microscopic observations (Dr. Lauren V. Ackerman, associate professor of surgical pathology and of pathology, Washington University School of Medicine): "No definite evidence of persistent leukosarcoma could be identified in any of the sections. The vertebral bone marrow was hypoplastic; it demonstrated some phagocytosis of hemosiderin, and there were a few large cells which could not be identified. There was also some proliferation of the reticuloendothelial cells. There was prominent hemosiderosis of the liver, and this was confirmed by an iron stain. This iron pigment was widely distributed through the liver lobules and was associated with increased fibrosis, which was particularly prominent in the portal areas. In these areas there was also some bile duct proliferation. Hemosiderosis was also present in the spleen, in a single lymph node, and there was deposition of hemosiderin pigment in the tips of the villi of the duodenum. The hemosiderosis was probably related to the numerous transfusions which this patient had received. In the periadrenal fat, in the wall of the duodenum and in a small section of pancreas there was a diffuse, acute inflammation. This inflammatory exudate was particularly prominent in the small section of the pancreas. Most of the cells making up this exudate were polymorphonuclear leukocytes, and in this single section the process could be designated as suppurative pancreatitis. There were small foci of lipoid pneumonia in the lung. These were minimal in extent and probably bore no relation to this patient's death. There were also focal collections of giant cells in the lung. Within the nuclei of these cells there were large acidophilic inclusions, which Dr. Margaret Smith of the Department of Pathology identified as compatible with salivary gland virus infection (these inclusions were found in a few cells within the liver and within the spleen so that probably there was fairly widespread diffusion of salivary gland virus). It is doubtful whether the presence of this virus had anything to do with the patient's death, and it was probably a terminal phenomenon."

Another one of our patients, a boy aged 4, with the same type of acute leukemia, has now been in fairly complete remission for twelve months, and the percentage of leukemic lymphocytes in the bone marrow decreased from 95 per cent to 5 to 10 per cent. However, the foregoing case was reported in detail because we wish to emphasize not the occasional spectacular

remission but rather the fact that most remissions induced by the folic acid antagonists are incomplete and of brief duration.

Two patients in the terminal phase of chronic myelocytic leukemia treated in our clinic with amino-an-fol showed no improvement, although in 1 patient the leukocyte level dropped temporarily. As no reports have yet been published on the effects of folic acid antagonists on chronic leukemia in the terminal phase, where the number of blast cells and other immature forms in the bone marrow simulates the observations in acute leukemia, an instance of this is summarized:

L. R., a man, aged 35, was first observed on February 28, 1947, because a blood cell count had revealed an elevated leukocyte level. He was asymptomatic, and there were no abnormal physical observations. The white blood cell count was 24,500; the erythrocyte count, hemoglobin value, and thrombocyte level were all within normal limits. The differential count showed 42 segmented neutrophils, 9 stab cells, 7 metamyelocytes, 26 myelocytes, 4 basophils and 11 lymphocytes. Sternal bone marrow examination revealed changes characteristic of chronic myelocytic leukemia. No therapy was given at that time.

A month later, in March 1947, he had influenza, after which progressive weakness and fatigability developed. The leukocyte level rose progressively to 57,000 by May 20, 1947. He also had a mild anemia, and the spleen became palpable. Radioactive phosphorus therapy was started, and from April 1947 to February 1948 he received a few injections of P^{32} every two or three months. During this ten month period his leukocyte level ranged between 20,000 and 60,000, and he felt well except for occasional fatigue.

From March 1948 until his death in January 1949, the disease ran a subacute course. Therapy and hematologic data during this period are recorded in figure 2. Administration of P^{32} was continued during March and April, 1948; fairly frequent large doses were given, and the leukocyte count dropped from 100,000 on March 2 to 42,000 on April 14. By this time the patient had received so much radioactive phosphorus that we decided to give urethane in the hope that this would at least decrease the amount of radiation required. Urethane caused rather severe nausea and vomiting, and it was impossible to maintain an effective dose.

During August 1948 the leukocyte level rose to 193,000 and the patient had fever, anorexia, nausea and extreme weakness. With intensive P^{32} therapy the leukocyte count dropped to 16,000 and he felt considerably better.

From August 30 to September 10 the white cell level increased from 16,000 to 81,000, and prostrating weakness recurred. Nitrogen mustard (methyl-bis[2-chloroethyl]amine hydrochloride) therapy was given September 13 and 15. Within a period of six days the leukocyte count decreased from 127,000 to 10,000, but there was no significant symptomatic improvement; the hematologic improvement lasted only a few days.

Aminopterin therapy (2 mg. intramuscularly daily) was started on Oct. 11, 1948; on October 18, because of increased nausea and vomiting, the doage was decreased to 2 mg. every other day. Within a period of three weeks the leukocyte count decreased from 180,000 to 18,000, but this was accompanied with such severe abdominal pain and vomiting that treatment had to be discontinued. Occasional injections of P^{32} were given thereafter, and the patient died Jan. 12, 1949.

The accompanying table summarizes the reported experience to date with folic acid antagonist therapy of acute leukemia. In addition, Berman and associates [51] treated 5 patients with chronic myelocytic leukemia and 4 patients with chronic lymphocytic leukemia with aminopterin, and Meyer [52] treated 3 patients with chronic myelocytic leukemia and 3 with chronic lymphocytic leukemia; none of these patients showed any significant clinical improvement.

Most investigators using these drugs have observed more frequent remissions of acute leukemia in infants and children than in adults. However, Wiseman [53] treated 36 patients with aminopterin and observed about the same remission rate for adults and children in acute lymphocytic leukemia; the results in acute monocytic leukemia were much less favorable, and no improvement occurred in any of his cases of acute myelocytic leukemia. All the remissions observed by us were confined to acute lymphocytic leukemia with the exception of a transient remission (about two weeks) which occurred in 1 case of acute myelocytic leukemia.

The severe toxic reactions produced by these drugs have been emphasized by all investigators. Stomatitis, ulceration of the mucous membranes of the mouth, diarrhea and gastrointestinal hemorrhage may occur. Leukopenia, thrombopenia and aplasia of the bone marrow are seen rather frequently, and sometimes these changes appear after relatively small doses of the folic acid antagonists.

Folic Acid Antagonist Therapy of Acute Leukemia

Principal Investigator	Drug Employed	Number of Patients Treated	Percentage of Significant Remissions
Farber [49]	Aminopterin Amethopterin Amino-an-fol	69	29
Stickney, J. M.; Hogeboom, A. B.; Mills, S. D., and Cooper, T.: Proc. Central Soc. Clin. Research 21:82, 1948	Aminopterin	18	28
Lovis, W. C.; Jacobson, W., and Rich, G.: Proc. Central Soc. Clin. Research 21:82, 1948	Aminopterin Amethopterin	20	20
Pierce, M., and Alt, H.: Proc. Central Soc. Clin. Research 21:82, 1948	Aminopterin	11	45
Dameshek, W.: Blood 4:162, 1949	Aminopterin Amethopterin Amino-an-fol A-cinoptorin	34	35
Meyer [52]	Aminopterin	27	11
Klingberg, W. G., and Cooke, J. V.: Personal communication to the authors	Aminopterin Amino-an-fol	18	39
Reinhard, Good and Martin....	Aminopterin Amino-an-fol	17	35

In spite of the severe toxicity of these drugs the evidence is convincing that temporary remissions of acute leukemia occur in a significant percentage of patients receiving such therapy; the preliminary suggestion is made that results may be better in children than in adults and better in acute lymphocytic leukemia than in other types of acute leukemia.

NITROGEN MUSTARDS

During World War I considerable work was done on the toxicology of mustard gas. Interest centered chiefly on its vesicant action and the resultant deep skin ulcers, conjunctivitis, laryngitis, bronchitis and secondary pneumonia,[54] but systemic effects on the gastrointestinal tract,[55] and particularly on the bone

51. Berman, L.; Axelrod, A. R.; Vander Heide, E. C., and Sharp, E. A.: Use of a Folic Acid Antagonist in Chronic Leukemia, Am. J. Clin. Path. 19:127, 1949.

52. Meyer, L. M.; Fish, H.; Sawitsky, A.; Rowan, M., and Ritz, N. D.: Aminopterin (A Folic Acid Antagonist) in the Treatment of Leukemia. Am. J. Clin. Path. 19:119, 1949.

53. Wiseman, B. K.: Personal communication to the authors.

54. Mandel, M., and Gibson, W. S.: Clinical Manifestations and Treatment of Gas Poisoning, J. A. M. A. 69:1970 (Dec. 8) 1917. The Pathology of "Mustard Gas," editorial, ibid. 70:1947 (June 22) 1918.

55. Warthin, A. S., and Weller, C. B.: The Medical Aspects of Mustard Gas Poisoning, St. Louis, C. V. Mosby Company, 1919. Lynch, V.; Smith, H. W., and Marshall, E. K., Jr.: On Dichlorethyl Sulfide (Mustard Gas): I. The Systemic Effects and Mechanism of Action, J. Pharmacol. & Exper. Therap. 13:265, 1918-1919.

marrow with resultant leukopenia,[56] were recognized. With the onset of World War II intensive study of mustard gas and related compounds was resumed. Mustard gas is bis (2-chloroethyl) sulfide. Two nitrogenous analogues of this compound were investigated; methyl bis- and methyl tris-(2-chloroethyl) amines, the so-called nitrogen mustards. Most of the clinical work on the treatment of neoplasms has involved the use of methyl bis (2-chloroethyl) amine hydrochloride, and hereafter in this paper the term nitrogen mustard will refer to this compound.

Gilman and Philips [57] have reviewed the complex chemistry and the pharmacologic effects of the mustards. It has been shown that these compounds exert a specific nucleotoxic action by interfering with chromosomal mechanisms and mitotic division in a manner somewhat analogous to the effects of roentgen rays. The susceptibility of cells to the lethal effect of the mustards is related to the rate of cellular multiplication, and presumably this explains, at least in part, the vulnerability of the bone marrow, lymphatic tissues and mucosa of the gastrointestinal tract. Nitrogen mustard produces cellular fragmentation in lymph nodes within ten hours, followed later by lymphatic atrophy. In the bone marrow early changes include altered staining reaction of the hemopoietic cells followed by progressive aplasia. In the intestines early vacuolization and nuclear swelling of the epithelial cells lead eventually to necrosis and desquamation with hemorrhage.[57]

Goodman and co-workers [58] and Jacobson and his associates [59] reported striking benefit from the administration of the nitrogen mustards to patients with malignant lymphomas and allied disorders. Dosages and technic of administration are discussed in these papers. Since then, more than seventy articles have been published on the clinical uses of nitrogen mustard. Gellhorn and Jones [17] have reviewed this literature and have tabulated an extensive bibliography. They found that favorable responses to nitrogen mustard therapy have been reported in Hodgkin's disease, lymphosarcoma, giant follicular lymphoma, chronic lymphocytic leukemia, chronic myelocytic leukemia, polycythemia vera, rhabdomyosarcoma, mycosis fungoides and anaplastic cancer of lungs; equivocal responses have been reported in lymphoepithelioma, Boeck's sarcoid, disseminated lupus erythematosus, neuroblastoma and Ewing's tumor; no response has been observed in acute leukemia, aleukemic leukemia, central nervous system tumors, squamous cell carcinoma of the lung, carcinoma of the genitourinary or gastrointestinal tract and oral cavity, carcinoma of the breast, melanosarcoma, fibrosarcoma, Kaposi sarcoma, osteogenic sarcoma and reticulum cell sarcoma. Subsequent reports [60] not included in the foregoing review do not significantly alter these conclusions.

We have treated 75 patients with nitrogen mustard, of whom 40 had Hodgkin's disease, 6 lymphosarcoma, 4 reticulum cell sarcoma, 9 carcinoma of the lung, 4 chronic leukemia, 3 mycosis fungoides and the remainder, miscellaneous malignant tumors. In spite of occasional transient clinical improvement at times associated with objective evidence of decrease in tumor size in various malignant neoplastic diseases, it is believed that our experience together with the data in the literature justifies the statement that nitrogen mustard is of definitely proved value only in Hodgkin's disease and, to a lesser extent, lymphosarcoma. Although favorable responses certainly occur in other lymphoblastomas, chronic leukemias, polycythemia vera, mycosis fungoides and anaplastic carcinomas of the lung, evidence is not convincing that nitrogen mustard is superior to roentgen radiation or other forms of therapy for these conditions in ordinary circumstances. Nitrogen mustard does not produce edema in tumor tissue such as is common after radiation, and it may be the treatment of choice when an anaplastic tumor is producing pressure on a vital organ. We have observed dramatic though transient relief of dyspnea in a patient with anaplastic carcinoma of the lung with metastases surrounding and constricting the trachea. Isolated instances of this sort do not invalidate the foregoing generalization.

It has been clearly established that in Hodgkin's disease following nitrogen mustard administration there is often a strikingly rapid return of temperature to normal, an improvement in appetite and a general sense of well-being; within a week or two enlarged nodes, spleen and liver may decrease decidedly in size, and other symptoms may improve.

Nitrogen mustard therapy has the following disadvantages: (1) it cannot be applied locally; (2) profound depression of bone marrow function is common even with therapeutic doses and is so severe that the subsequent leukopenia and thrombopenia may endanger the patient's life, and (3) it is generally agreed that remissions are shorter than those induced with roentgen radiation. According to Rhoads [61] the average remission lasts only one month, and certainly remissions lasting longer than three or four months are rare. The average remission following fifty-nine courses of nitrogen mustard therapy which we gave to 33 patients with Hodgkin's disease was approximately seven weeks. Because of these disadvantages, it is now generally agreed that roentgen therapy is the treatment of choice for localized Hodgkin's disease with minimal or no systemic manifestations. However, treatment with nitrogen mustard should be considered: (1) when the patient has been given an adequate course of roentgen radiation and the palpable and radiologically demonstrable lesions have failed to respond because repeated roentgen courses in the past have rendered them "roentgen fast"; (2) when trophic skin changes from repeated

56. Krumbhaar, E. B., and Krumbhaar, H. D.: The Blood and Bone Marrow in Yellow Cross Gas (Mustard Gas) Poisoning, J. M. Research 40:497, 1919.

57. Gilman, A., and Philips, F. S.: The Biological Actions and Therapeutic Applications of the β-Chloroethyl Amines and Sulfides, Science 103:409, 1946.

58. Goodman, L. S.; Wintrobe, M. M.; Dameshek, W.; Goodman, M. J.; Gilman, A., and McLennan, M. T.: Nitrogen Mustard Therapy. Use of Methyl Bis (β-Chloroethyl) Amine Hydrochloride and Tris (β-Chloroethyl) Amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders, J. A. M. A. 132:126 (Sept. 21) 1946.

59. Jacobson, L. O.; Sparr, C. L.; Barron, E. S. G.; Smith, T.; Lushbaugh, C., and Dick, G. F.: Nitrogen Mustard Therapy: Studies on the Effect of Methyl Bis (β-Chlorothyl) Amine Hydrochloride on Neoplastic Diseases and Allied Disorders of the Hematopoietic System, J. A. M. A. 132:263 (Oct. 5) 1946.

60. Karnofsky, D. A.; Ahlman, W. H.; Craver, L. F., and Burchenal, J. H.: The Use of the Nitrogen Mustards in the Palliative Treatment of Carcinoma: With Particular Reference to Bronchogenic Carcinoma, Cancer 1:634, 1948. Goldman, R.; Egeberg, R. O.; Ware, E. R.; Evans, E. R., and Pishkin, B. G.: Clinical Experience with Nitrogen Mustard Therapy, Arch. Int. Med. 82:125 (Aug.) 1948. Shullenberger, C. C.; Watkins, C. H., and Kierland, R. R.: Experience with Nitrogen Mustard Therapy, J. A. M. A. 139:777 (March 19) 1949. Bruns, A. M., and Jacobson, L. O.: Comparative Therapeutic Effects of Radioactive and Chemical Agents in Neoplastic Disease of the Hemopoietic System, Am. J. Roentgenol. 58:774, 1947. Henstell, H. H., and Tober, J. N.: Treatment of Mycosis Fungoides with Nitrogen Mustard, J. Invest. Dermat. 9:183, 1947. Emerich, R.: Observation of Nitrogen Mustard Therapy, Harper Hosp. Bull. 6:118, 1948. McHugh, J. M., and Ziehl, F. L.: Nitrogen Mustards in Neoplastic Diseases, Marquette M. Rev. 13:56 and 100, 1948. Dameshek, W.; Weisfuse, L., and Stein, T.: Nitrogen Mustard Therapy in Hodgkin's Disease, Blood 4:338, 1949. Kurnick, N. B.; Paley, K. R.; Fieber, M. H., and Adler, D. K.: Treatment of Malignant Disease with Nitrogen Mustard, Ann. Int. Med. 30:974, 1949. Meyer, A. H., and Overmiller, W. C.: The Use of a Nitrogen Mustard in Hodgkin's Disease and Lymphosarcoma, ibid. 30:381, 1949. Ben-Asher, S.: Nitrogen Mustard Therapy, Am. J. M. Sc. 217:162, 1949.

61. Rhoads, C. P.: Recent Advances in Treatment of Cancer, J. A. M. A. 139:305 (Jan. 21) 1948.

(Footnote 60 continued in next column)

courses of roentgen radiation preclude the further use of such therapy (in these circumstances, nitrogen mustard may be the treatment of choice even though the tumor remains sensitive to radiation), and (3) in those cases of Hodgkin's disease characterized by high fever, sweats, malaise, generalized aching pains, anorexia, weight loss and pruritus unaccompanied with pronounced localized enlargement of lymph nodes, splenomegaly or hepatomegaly.

SUMMARY

The data in the literature and our experience would appear to justify the following conclusions. Serratia marcescens polysaccharide is a potent carcinolytic substance, but it produces such severe toxic reactions that its general clinical use cannot be recommended. The original enthusiastic reports on KR and antireticular cytotoxic serum have not been completely confirmed by later investigators, and final evaluation of these substances must be held in abeyance. Urethane has been found to be effective in the treatment of chronic leukemia but is probably not as satisfactory as radiation therapy (roentgen ray or P^{32}) in most instances. Temporary remissioins in acute leukemia can be produced in 25 to 50 per cent of cases by administration of folic acid antagonists such as aminopterin, but no cures have been observed and remissions usually last only a few weeks to several months. Roentgen radiation remains the treatment of choice for localized Hodgkin's disease or lymphosarcoma, but nitrogen mustard is a valuable adjunct to radiation therapy in the diffuse form of these lymphomas and in those instances in which the lesions have become "roentgen fast" or when trophic skin changes from previous intensive radiation preclude the further use of roentgen rays.

ABSTRACT OF DISCUSSION

DR. J. M. STICKNEY, Rochester, Minn.: Dr. Reinhard has covered a large subject thoroughly. As far as I am aware, no chemotherapeutic agent has proved to be curative in malignant disease, and in the absence of a cure the evaluation of these agents must depend on the analysis of remissions or of survival times. It is unfortunate that in these diseases good control studies are difficult to find. I should like to summarize my experience at Mayo Clinic with the folic acid antagonists in acute or severe subacute leukemia. We have used aminopterin more than any of the other substances and have treated 54 patients with it. Twenty-one of these patients were 14 years of age or younger. In 5 of these 21 we observed what we called complete hematologic and clinical remissions and in 5 more we noted partial remissions which were principally clinical. In no instance did a remission last more than four months. We were able to induce subsequent remissions, after the first remission had disappeared, in only 1 patient. Of 33 adults with acute leukemia only 3 had complete remissions, and none of these have been maintained hematologically more than ten to twelve weeks, although clinical remissions have lasted much longer than that. Partial remissions have been seen in 3 more. It is our opinion that acute leukemia of all cell types responds to the folic acid antagonists. We believe that these substances actually produce remissions in acute leukemia, but we have not seen completely normal bone marrow. In 6 cases of chronic lymphocytic leukemia in the acute terminal stage these drugs have been useless. If these compounds (to some extent, at least) act because of their folic acid antagonism, it is surprising that megaloblastic bone marrow is not produced more often. We have observed it, but at no time does the number of megaloblasts approach that seen in pernicious anemia. We have had some experience with aminopterin in treatment of patients with malignant disease but have not been impressed with the results. The patients have been especially susceptible to the toxic effects of the drug, which have seemed to occur much earlier and oftener than in patients with acute leukemia. Urethane may be an excellent compound for use in chronic myelocytic leukemia, particularly if the patients are not near roentgen treatment centers. Nitrogen mustards are adjuncts to roentgen therapy, but in our experience the remissions in Hodgkin's disease following treatment with nitrogen mustard are not as long sustained as those obtained with roentgen therapy. The remissions in polycythemia vera treated with nitrogen mustard are not as long sustained as those induced by radioactive phosphorus.

DR. WILLIAM DAMESHEK, Boston: Nitrogen mustard has become an indispensable therapeutic tool in hematologic practice, particularly in the management of Hodgkin's disease and disseminated lymphosarcomatosis. Its rapid "detoxifying" action is probably due largely to the intravenous route of administration with resultant widespread activity against all abnormal tissue. Its chief value lies in the cases of disseminated Hodgkin's disease when the patient has constitutional manifestations. In these cases it often produces striking remissions and relieves many patients for varying periods of time. Some patients with disseminated, roentgen-refractory lymphosarcoma respond brilliantly and have prolonged remissions lasting for six months to a year and a half following a single course of nitrogen mustard therapy. I have found urethane to be of definite value in prolonging and maintaining the roentgen-induced remission in chronic myelocytic leukemia. It allows the internist to control the patient's therapy; this is often better than divided control with a radiologist. The dosage of the drug can be readily adjusted to the patient's leukocyte count and symptoms. More than 3 Gm. daily of the keratin-coated tablets are seldom necessary. The drug is also of great value in a goodly proportion of patients with multiple myeloma (plasmacytic leukemia). In the patients reacting favorably, bone pains are relieved, spontaneous fractures may heal, the proteins in the blood may recede to normal and the bone marrow may become normal or nearly so. The folic acid antagonists are often of distinct value in the treatment of acute and subacute leukemia, both in children and in adults. Remissions are obtained in about one third of the cases; these last from two to several months. Best effects are obtained in acute lymphocytic leukemia, the worst effects in acute monocytic leukemia. In acute monocytic leukemia I have obtained remissions in some cases with a form of nitrogen mustard called SK-136, which is N,N',N'-tetrakis (2-chloroethyl)-1,3-propanediamine dihydrochloride. With aminopterin therapy, the drug is given until the patient gets a definite reaction; administration of the drug is then stopped; it is then resumed if the patient improves, after which maintenance therapy is given daily and usually continuously. I have also used the drug in the myeloblast crisis of chronic myelocytic leukemia with distinct remission in 1 case.

DR. M. J. SHEAR, Bethesda, Md.: As Dr. Reinhard stated, these bacterial polysaccharides with specific effect on certain types of tumors are not recommended for clinical use. They constitute laboratory curiosities. As such, they are of considerable interest, but they are not useful clinically. The mechanism of their action is still obscure. Whether one works with the polysaccharide isolated from Escherichia coli or from Bacillus prodigiosus, or with crude preparations from a considerable number of other gram-negative organisms, the mechanism by which tumor tissue is damaged is still a subject of speculation. Shock supervenes in many cases, both in animals and in human beings, but it is an open question whether the shock is a necessary prerequisite for destruction of tumor tissue or an aftermath of incidental side effects which perhaps in the future might be obviated. As Dr. Reinhard has said, the material is toxic; and although efforts are being made in the laboratory to reduce the toxicity, the biggest obstacle is its antigenicity. These agents provoke antibodies, and the greatest destructive effect on the tumors is obtained with the first injection. Subsequent injections, even two or three days later, produce little detectable effect on the tumors. This phenomenon has been under study by Drs. Creech, Wharton and others at the Institute for Cancer Research in Philadelphia, and they have been able to isolate antibodies not only of a classic sort which appeared after some weeks, but an unexpected kind of antibody which appeared

within two or three days after the first injection. Dr. Reinhard mentioned that the incidence of spontaneous remissions in acute leukemia in children at his institution was considerably smaller than the series of cases referred to by Dr. Farber in the work of Dr. Louis Diamond at the Children's Hospital in Boston. Among several hundred children with untreated acute leukemia in Boston, brief remissions were observed in 9.5 per cent of the cases. The point that I wish to highlight is that in three fourths of these cases of spontaneous remission, the remissions were preceded by an episode of acute infection. Remarkable progress is being observed in the control of infectious diseases. Concurrently, and apparently unrelatedly, there is an increase in the incidence of malignant diseases even when figures are corrected for improved methods of diagnosis and for age distribution. Are pathogenic and nonpathogenic microorganisms one of Nature's controls of microscopic foci of malignant tissue, and, in making progress in the control of infectious diseases, are we removing one of Nature's controls of cancer?

FALSE POSITIVE REACTIONS TO THE SCHICK TEST

Incidence and Interpretation

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It has been known almost since active diphtheria immunization was begun that systemic reactions to diphtheria inoculations were more common among adults than among children. Since 1928 the Moloney test[1] has made it possible to detect many of these potential reactors. Because there has been little or no adult immunization since the widespread introduction of immunization in childhood, the problem of reactions has never been a serious one. However, with the recently increasing consciousness of the potential danger of a nonimmune adult population,[2] immunization procedures among young adults may be indicated in suitable circumstances.

The results of this study appear to demonstrate that the great majority of severe systemic reactions are avoidable, since they occur in immune persons who needed no immunization. They indicate also that the reaction to the ordinary Schick test, when positive, is not a completely reliable index of susceptibility to diphtheria.

METHODS

Young pregnant women attending the prenatal clinic of the Beth Israel Hospital, New York, were routinely Schick-tested as part of the admission procedure. Materials used were standard preparations available commercially.[3] The Schick test was performed in the routine manner in the skin of the left forearm, and the control test was made in the skin of the right forearm. A Moloney test, using purified diphtheria toxoid of standard immunizing strength diluted 1:20 with isotonic sodium chloride solution, was also performed in the skin of the right forearm. Readings were made seven days after the tests were performed, and blood was drawn at this time for titration of circulating diphtheria antitoxin. Women who had had both positive and negative reactions to the Moloney test, were given a full immunization course with diphtheria toxoid. Readings of the skin tests were made in accordance with the criteria of Schick.[4] All patients who had doubtful readings were excluded from the series.

TABLE 1.—*Comparison of the Circulating Diphtheria Antitoxin Titer and the Reactions to the Schick Test in 114 Women*

Reaction to Schick Test	Total Cases	Titers Over 0.01 Unit	Titers Under 0.01 Unit	Percentage
Negative	32	31	..	96.9
Positive	82	..	63	77.4

RESULTS

A total of 114 women were compared with regard to Schick test and circulating diphtheria antitoxin titer. The results are shown in table 1. It is evident that while a negative reaction to the Schick test almost always means that there is more than 0.01 unit of circulating diphtheria antitoxin per cubic centimeter of blood, in only 3 cases of 4 with postive Schick skin reactions, was there less than 0.01 unit circulating antitoxin per cubic centimeter of blood.

The patients in cases in which there was no agreement between the results of the Schick test and circulating antitoxin titers were then examined individually, and the following conditions were common to all: 1. Schick reaction was only moderately positive—seldom strongly positive. 2. Reaction to the control test was negative. 3. The Moloney reaction was always positive, usually strongly so. 4. Circulating antitoxin titers were high, in many cases higher than expected after active immunization. 5. All these immunized patients had exhibited moderate to severe systemic reactions, as shown in the following outline.

TABLE 2.—*Conditions Common in All Cases in Which There Was No Agreement Between the Circulating Antitoxin Titers and the Reaction to the Schick Test*

Case No.	Age (Years)	Previous Immunization	Tests			Reaction*	Titers
			Schick	Control	Moloney		
1	22	Diphtheria in childhood	++	–	+++	Extremely severe	10+ 25–
2	21	Unknown	++	–	++	Severe	10+ 25–
3	19	Diphtheria at age 11	++	–	+	Severe	1+ 10–
4	42	None	++	–	+	Moderate	2.5+ 5.0–
5	30	None	++	–	+	Severe	5.0+ 12.5–
6	22	Diphtheria in childhood	++	–	+++	Extremely severe	2.5+ 5.0–
7	29	None	++	–	++++	Severe	1– 10–
8	24	None	+	–	++++	Moderate	1+ 10–
9	41	None	++	–	+	Moderate	1+ 10–
10	25	Immunized in childhood	++	–	+	N. I.	10+ 25–
11	32	Immunized in childhood	++	–	++++	N. I.	1+ 10–
12	28	None	+++	+	++++	N. I.	1+ 10–
13	27	None	++++	+	++++	N. I.	1+ 10–

* N. I. means not immunized.

Mild reactions:

1. Redness, heat and itching
2. Swelling around area of injection

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1. Moloney, P. J., and Fraser, C. J.: Preparation de l'anatoxine diphtherique et verification de ses proprietes, Ann. Inst. Pasteur 42:1430, 1928.

2. Cohen, P.; Schneck, H.; Dubow, S., and Cohen, S. O.: The Changed Status of Diphtheria Immunity, Pediatrics 5:630, 1949.

3. Parke, Davis & Company.

4. Schick, B., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1944, vol. 2, chap. 4, p. 4.

Moderate reactions:

3. Local pain and tenderness
4. Swelling of arm
5. Headache
6. Malaise and anorexia
7. Low grade temperature, not maintained for more than 24 hours (100 to 101 F.)

Severe reactions:

8. High temperature, maintained for more than 24 hours (103 to 105 F.)
9. Chills
10. Weakness and collapse

The complete results are presented in table 2.

Color photographs were taken of a number of patients at the time that readings were made. Those patients selected for photographing had the features previously described, that is, a moderately positive Schick reaction, a negative reaction to the control test and a strongly positive Moloney reaction. Titers taken at the time of reading proved high in all cases, demonstrating the false positive Schick reactions (figs. 1, 2 and 3).

Fig. 1 (case 13 in table 2).—In this figure and in figures 2 and 3 the reaction to the Schick test is on the left arm and the Moloney and control tests on the right arm, the latter being represented by the small spot below the large positive Moloney reaction. The circulating antitoxin titer in this case was between 1 and 10 units per hundred cubic centimeters of blood.

COMMENT

Evidently a considerable number of positive reactors to the Schick test, as judged by the standard method of performing the test, are not truly susceptible to diphtheria. Brandon and Fraser[5] reported this fact in 1936. They stated, ". . . certain controls of the heated toxin variety did not elicit nearly as large reactions as the corresponding toxins." No explanation was given for this, nor has any been forthcoming since, but it is plausible to assume that the heating process used in destroying the diphtheria toxin so alters the other proteins present that they are no longer capable of causing the reactions of the unheated material. Brandon and Fraser advocated the use of a diluted toxoid control similar to the one used in the Moloney test. One of us (P. C.) has on many occasions given children several series of diphtheria toxoid injections only to find that the Schick reaction was persistently positive. It was also noted that there was a familial tendency in this apparent failure of immunization to diphtheria. In the light of the present work, the interpretation of this is that sensitivity to the diphtheria toxoid or diphtheria protein yielded false positive reactions. In the future it may be advisable in such cases not to rely on the Schick test, the reaction to which

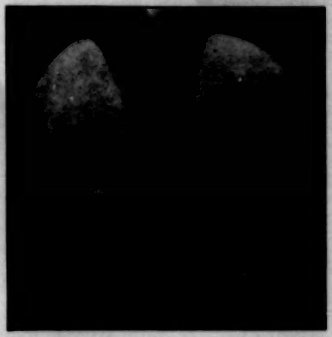

Fig. 2 (case 12 in table 2).—The circulating antitoxin titer in this case was between 1 and 10 units per hundred cubic centimeters of blood.

may remain falsely positive, but to pursue blood antitoxin titrations.

Lawrence and Pappenheimer[6] have separated and studied the toxin-toxoid and protein fractions from cultures of the diphtheria bacillus. The same authors[7] have demonstrated that either of these substances may be responsible for specific allergic reactions of the delayed tuberculin type and, therefore, for a false positive Schick reaction but that many more of these reactions were due to toxoid than to protein fraction. (In

Fig. 3 (case 10 in table 2).—The circulating antitoxin titer in this case was between 10 and 25 units per hundred cubic centimeters of blood.

the case of toxin, the false reactions may be due to the natural toxoid content of this material as it is formed in cultures.)

5. Brandon, K. F., and Fraser, D. T.: Observations on Interpretations of Schick Tests: Comparison of Schick Test Interpretations Using Different Products on the Same Individual Simultaneously, J. Immunol. 31: 387, 1936.

6. Lawrence, H. S., and Pappenheimer, A. M., Jr.: Immunization of Adults with Diphtheria Toxoid: I. Immunological Properties of Formalinized Diphtherial Protein Fractions from Culture Filtrates, Am. J. Hyg. 47: 226, 1948.

7. Pappenheimer, A. M., Jr., and Lawrence, H. S.: Immunization of Adults with Diphtheria Toxoid: II. An Analysis of the Pseudoreactions to the Schick Test, ibid. p. 233.

Ideally then, the Schick test should be done with two controls, one of toxoid and the other of diphtheria protein material, and the present heated toxin control material should be discarded. Another alternative, suggested by Ross,[8] is the use of a purified toxin solution, so prepared as to require no control when used in the Schick test. This material appears to need further standardization and comparison with present procedures before it can be put into widespread use.

SUMMARY

1. A considerable number of Schick-tested persons whose reactions to the standard Schick test and control have been interpreted as positive have high titers of circulating antitoxin. Instead of being susceptible to diphtheria they may actually have a high potential of immunity, either from adequate circulating diphtheria antitoxin or from rapid development of circulating antitoxin through the stimulus of the Schick material alone (anamnestic recall).

2. These persons demonstrate characteristic features, a moderately positive Schick reaction, a negative reaction to the control test and a strongly positive Moloney reaction.

3. When given a series of immunizing injections, these persons experience severe systemic reactions.

4. The present Schick test technic is significant if the reaction is negative, but there is a certain percentage of inaccuracy in positive reactions. Changes are indicated in control materials or in test materials to eliminate this error.

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TRIGEMINAL INJECTION WITH RADIOGRAPHIC CONTROL

Technic and Results

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For a large group of patients with pain referable to the face, interruption of the nervous pathway from the painful area appears to be the best available therapy. Those persons with idiopathic trigeminal neuralgia or with malignant neoplasms of the face compose the largest number of such patients, but, in addition, persons with more obscure forms of facial pain may with profit undergo diagnostic trigeminal injection. The production of temporary analgesia of the appropriate trigeminal division is perhaps advisable in the majority of instances prior to any permanent operative section. The advantages of such a procedure have been summarized by Cushing,[1] Adson,[2] Grant,[3] Jefferson [4] and Horrax and Poppen,[5] among others. These advantages are said to be threefold. First, the prognosis of relief by operation can be given with virtual certainty. If an injection affords relief, an operation which is productive of the same analgesia will afford the same relief. On the other hand, if after injection the patient continues to have pain referable to the analgesic area, he will not be relieved by subsequent trigeminal operation. Few challenge this; however, Jaeger [6] states that he has seen relief of pain after section of the trigeminal posterior root in an area rendered anesthetic by alcohol injection but still painful. The second advantage of the production of temporary analgesia is that the duration of the numbness in the face following alcohol injection gives the patient ample opportunity to decide whether or not he prefers this sensation to his original pain. One or two recurrences of the original paroxysms may help the patient with trigeminal neuralgia to decide whether or not to accept the permanent numbness and paresthesias after operation in exchange for the pain. Peet and Echols [7] (page 253), however, consider this a poor excuse for performing injection. The third advantage is that in debilitated patients the injection may effect enough relief to permit a normal food intake with restoration of the general nutrition and health and diminution of the operative risk. In those likely to die soon, completion of the life span without operation may occur.

Although in numerous publications many technics are described for achieving block of the trigeminal branches, most authors neglect to mention the frequency with which they attain their objective. However, Patrick [8] reports that after five hundred extraoral subzygomatic injections he was successful at the first attempt in only 18 per cent of cases at either the foramen ovale or the foramen rotundum. Much higher figures were reported by Adson,[2] who said that the effort is rewarded in approximately 70 per cent of the cases in which injections were given and by Grant,[3] who was successful in 80 per cent of his injections into the second division and in 79 per cent of those into the third division.

The most succinct directions I know for the performance of trigeminal injection are those of Cushing,[1] who stated, "This is more or less of a gift, and there are no rules to follow. One introduces the needle to the nerve." More detailed instructions are contained in the writings of Harris [9] (pages 190 to 204), Grant [3] and Horrax and Poppen.[5] Grant in particular provides the novice with precise angles, both superoinferiorly and anteroposteriorly, for the introduction of the shaft of the needle.

Early in my own experience I became disturbed at the agony I was giving my patients as I probed with the needle, trying to elicit the complaint of pain in the proper peripheral distribution, and I agreed with Dandy [10] that the pain of injection is a terrible ordeal. I have been especially likely to fail in my attempts to find the third division. In an effort to make the injection less of a trial for all concerned, I began in 1940 to take roentgenograms showing the position of the needle point with respect to the foramen ovale when I had difficulty in finding the nerve, and in the past ten years I have used this technic in fifty-four instances with success in fifty-one. I have learned of the use

8. Ross, V.: Preparation of Diphtheria Toxin Solutions Requiring no Control in the Schick Test, J. Immunol. 50: 207, 1948.

Read before the Harvey Cushing Society, June 1949, in New Haven, Conn.

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1. Cushing, H.: The Role of Deep Alcohol Injections in the Treatment of Trigeminal Neuralgia, J. A. M. A. 75: 441 (Aug. 14) 1920.

2. Adson, A. W.: Trigeminal Neuralgia: Diagnosis and Treatment, S. Clin. North America 15: 1359 (Oct.) 1935.

3. Grant, F. C.: Alcohol Injection in the Treatment of Major Trigeminal Neuralgia, J. A. M. A. 107: 771 (Sept. 5) 1936.

4. Jefferson, G.: Observations on Trigeminal Neuralgia, Brit. M. J. 2: 879 (Nov. 14) 1931.

5. Horrax, G., and Poppen, J. L.: Trigeminal Neuralgia: Experiences with and Treatment Employed in Four Hundred and Sixty-Eight Patients During the Past Ten Years, Surg., Gynec. & Obst. 61: 394 (Sept.) 1935.

6. Jaeger, J. R., in discussion on Grant.[3]

7. Peet, M. M., and Echols, D. H.: Surgery of Disorders of Cranial Nerves, in Bancroft and Pilcher: Surgical Treatment of the Nervous System, Philadelphia, J. B. Lippincott Company, 1946.

8. Patrick, H. T.: The Technic and Results of Deep Injections of Alcohol for Trifacial Neuralgia, J. A. M. A. 56: 155 (Jan. 20) 1912.

9. Harris, W.: Neuritis and Neuralgia, London, Oxford University Press, 1926.

10. Dandy, W. E., in discussion on Grant.[3]

of this technic by a number of workers but have located no report in the literature describing the method or assessing its utility. The tiny pterygopalatine fossa in which the second trigeminal division lies has proved a more satisfactory landmark for blind injection in my hands, and I have had much less trouble in finding the

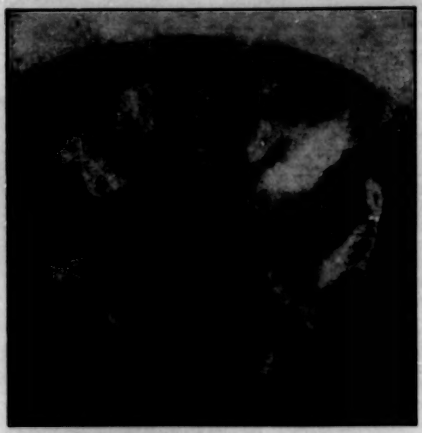

Fig. 1.—Needle point in the position at which injection of alcohol caused analgesia throughout domain of mandibular division.

second division. However, in 1943 I began, in cases of special difficulty, to use roentgenograms showing the position of the needle point with respect to the foramen rotundum. This procedure has permitted the making of nineteen successful injections of this nerve in nineteen attempts.

INJECTION INTO THE MANDIBULAR DIVISION

Method.—The technic which Grant [9] described so well was essayed as the point of departure in each patient. The method as now adopted involves the following steps. Preinjection medication of 16 mg. morphine sulfate is given subcutaneously, or even intravenously if the patient is exceedingly apprehensive. A 20 or 22 gage lumbar puncture needle with a short bevel is inserted through a wheal made with 1 per cent procaine hydrochloride below the zygoma at a point 2 cm. in front of the posterior bony margin of the condyle of the mandible. The needle is directed inward at a right angle with the anteroposterior plane of the zygoma, with the hilt sufficiently lower than the point so that the base of the skull is struck at a depth of 4 to 4.5 cm. The point is then lowered slightly and carried in to a depth of 4.5 to 5.5 cm., depending on my guess as to the width of the patient's skull. A radiograph yielding a basal view of the skull is then obtained, according to either of the two standard methods for doing so (Pancoast, Pendergrass and Schaeffer [11] page 47, or Orley [12] page 16). The needle is replaced in accordance with the error shown in the roentgenogram, and successive roentgenograms and placements are made until the point is seen overlying the foramen ovale (fig. 1). This has usually been the case on the second or third roentgenogram. Following the procedure of Harris [9] (page 213) in his injections of the gasserian ganglion, and that of Grant,[9] I use only alcohol after the needle is presumed to be in the desired position. I have found the injection into the nerve of 95 per cent alcohol, a drop at a time, to be little or no more painful than the injection of procaine hydrochloride, and analgesia produced by the alcohol is almost certain to last. If procaine hydrochloride is used initially, it may anesthetize the nerve by diffusing into it even though the needle point lies outside the nerve. The alcohol injected subsequently in these circumstances, however, appears not to follow the procaine hydrochloride into the nerve, and the sensory loss may endure but a few hours. After analgesia in a portion of the third division develops, it can be extended by appropriate rotation of the bevel of the needle. The fibers to the tongue lie in the anterior part of the nerve, and a forward direction of the bevel with further injection will anesthetize these if they escape initially. Conversely, the fibers to the lower lip and gum lie in the posterior part of the nerve. When analgesia of the third division has been produced by the injection of 0.3 to 2.0 cc. of alcohol, the needle is then rotated so that the bevel points upward, and more alcohol, 1 to 5 cc. for the whole injection, is slowly instilled. The purpose of the upward direction of the bevel is to encourage the alcohol to move superiorly into the ganglion, thereby lengthening the duration of the analgesia. The injection is stopped as soon as hypalgesia or analgesia in the zones of the first or second divisions is produced. At times, even though the roentgenogram shows the needle point to lie in the center of the foramen ovale, no analgesia follows the injection of 0.2 to 0.3 cc. of alcohol. A minimal increase or decrease in the depth of the needle usually suffices to permit analgesia to be secured. Even if the point lies near the front or back of the foramen ovale, a successful injection into the entire nerve trunk has usually been attained by appropriate direction of the bevel of the needle without one's changing the position of the entire shaft of the needle.

Reference of Pain at Time of Placement of Needle at Foramen Ovale (45 Cases)

	Cases
Reference to typical peripheral distribution of nerve	
Lower lip, lower jaw or tongue	12
In front of and above tragus	1
Whole side of face	2
Total	15 (33⅓%)
	Cases
Atypical reference	
Only at site of needle	18
Scattered areas other than at site of needle (ear, forehead, maxilla)	7
No pain	5
Total	30 (66⅔%)

REASONS FOR FAILURE WITHOUT ROENTGENOGRAMS

As my series of patients who were given injections under radiographic control increased, the reasons for many of my difficulties became clear. At the moment the needle is inserted into the nerve the patient is expected to complain of pain referred to the peripheral distribution of the nerve in the lower lip, tongue or

11. Pancoast, H. K.; Pendergrass, E. P., and Schaeffer, J. P.: The Head and Neck in Roentgen Diagnosis, Springfield, Ill., Charles C Thomas, Publisher, 1940.
12. Orley, A.: Neuroradiology, Springfield, Ill., Charles C Thomas, 1948.

upward from the posterior half of the zygoma. Only when the operator receives this cue from the patient may he be reasonably certain that the needle is placed correctly, if roentgenograms are not used. In fact, when the needle was placed in the proper position (as indicated both by roentgenograms and by the development of analgesia when alcohol was injected), the patient's description of his sensation varied greatly from case to case (table). Of the 45 patients in whom a specific note was made on this point, only 12 complained of pain referable to the lower lip, lower jaw or tongue. In 1 patient pain was felt in a small area in front of and above the tragus, and in 2 patients there was a severe pain throughout the whole side of the face. But in none of the remaining 30 of the group was there any clearcut cue that the nerve might have been penetrated. In 18 patients the pain was described as being only at the site of the needle, a sensation which most of them had also when the needle was nowhere near the nerve. There were 5 who felt no pain at all. In the remainder the reference of pain varied as follows:

Fig. 2.—*A*, continuous line at 115 degrees represents the angle with the plane joining the side of the skull and the zygoma. Interrupted line at 75 degrees represents the angle with the plane joining the posterior part of the body of the mandible and the zygoma. *B*, angle in the sagittal plane along the length of the zygoma.

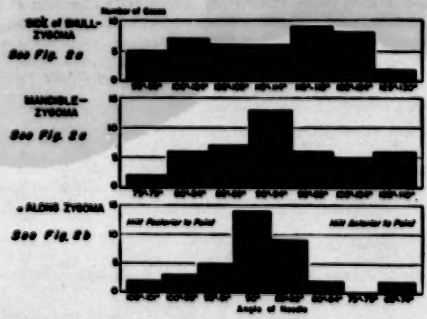

Fig. 3.—Histograms showing the actual angles measured with the needle point in a position for successful injection of alcohol into the mandibular division.

to the ear in 2 patients; the forehead, the malar region, the maxilla, upward from the anterior half of the zygoma and the side of the scalp behind the orbit plus the posterior cervical region in 1 case each. In every one of these 45 cases the injection of the first fraction of 1 cc. of alcohol caused sensory loss only in the area supplied by the mandibular division, evidence that the needle was in fact within these particular nerve fibers. The site of reference of pain as this initial alcohol was injected was not a much more satisfactory indication that the fluid was going to the proper spot. Although a bare majority of the patients did then refer pain to one or more of the principal areas of supply of the mandibular division, others experienced pain only at the site of the needle, or pain in areas of the face or head outside the usual distribution of fibers of the third division, or no pain at all. Hence it would appear that those who rely on site of reference of pain to determine the correct placement of the needle may spear the nerve several times before the patient finally gives the desired answer, if indeed he ever does. Both Harris[9] (page 201) and Horrax and Poppen[8] mention that the patient may complain of pain only locally when the needle has struck the nerve, so that this observation is not peculiar to the patients in my group. The reference of pain to such places as the ear and the forehead suggests that many of the fibers in this nerve supply areas beyond its autonomous zone and extend into areas largely supplied by other nerves.

FAILURES WITH ROENTGENOGRAMS

In the 3 cases of the 54 in which treatment was considered a failure, only a part of the fibers of the third division was anesthetized. The problem was one of atypical facial pain in 2 cases, and in neither was the pain relieved. In the third case only moderate hypalgesia rather than analgesia was produced. This, however, relieved the patient completely of his typical trigeminal neuralgia for thirty months, and hence the treatment was as successful clinically as most injections which produce analgesia. In no case was the nerve missed entirely.

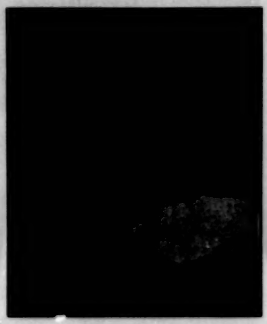

Fig. 4.—Position of tube, patient and film for demonstration of the foramina rotunda.

VALUE OF EXTERNAL LANDMARKS TO ASSIST PLACEMENT

The precise locus of the needle when correctly placed was measured in 42 of the cases. The angles made by the shaft of the needle with respect to three lines of reference were noted: first, the angle with the plane joining the side of the skull and the zygoma; second, the angle with the plane joining the posterior part of the body of the mandible and the zygoma, and third, the angle along the length of the zygoma (fig. 2).

The first angle varied from 95 to 130 degrees, and the second varied from 75 to 110 degrees. The drawing (fig. 2*A*) indicates that each of these angles is a measure of the position of the needle in the coronal planes. Neither angle is of crucial importance, but the more superiorly the point is directed, the greater the likelihood that it may go through the foramen ovale into the intracranial cavity instead of striking the medial

wall of the foramen. Histograms (fig. 3) show the distribution encountered over the full range.

The third angle, along the zygoma, varied from 65 to 105 degrees (fig. 2*B*). The histogram, however, shows that the great majority of the cases are clustered in the region of 5 degrees to either side of 90 degrees.

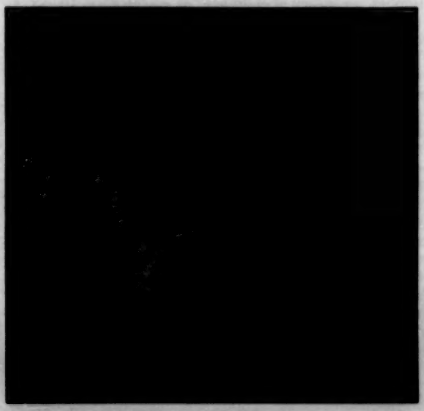

Fig. 5.—The arrows point to the foramina rotunda in an anatomic preparation of a skull in which fine wires were placed within the foramina.

This angle is important, and, if care is taken to insert the needle point through the skin precisely 2 cm. in front of the posterior bony margin of the condyle of the mandible, the variations will be diminished. In my series the depth of the needle varied from 3.8 to 5.1 cm. in the female patients and from 4.7 to 5.5 cm. in the male patients. The average depth among the women was 4.6 to 5.0 cm. It is apparent that measurements of angles and depths as done here constitute a useful basis for departure but cannot be relied on entirely for success. Possibly with more accurate cephalometry greater precision could be achieved, since there may prove to be a close correlation between the greatest width of the head and the depth of the foramen ovale.

DURATION OF RELIEF

The technic of keeping the bevel of the needle pointing upward during the latter part of the injection resulted in a spread of hypalgesia or analgesia into the zones of the first or second division in 23 of the 54 patients. Usually the sensory loss outside the third division lasted only a few days, but its presence suggested that the alcohol had penetrated to some of the cells of the gasserian ganglion, and this was borne out by the gratifying duration of the relief of pain. In the 30 patients with trigeminal neuralgia from whom replies to follow-up letters were received, the average duration of relief of pain was 30 months. Of this group 11 either have since died of intercurrent disease or are still free of pain, so that the duration of effective analgesia is even greater than 30 months. The average duration reported by Grant [5] was a little over 16 months and by Horrax and Poppen [6] 14.3 months. In the patients with malignant neoplasms about the face, the pain was felt over so wide an area that a total analgesia of the third division fibers relieved the pain for over 1 month in only one-eighth of the cases.

COMPLICATIONS

In 2 patients a temporary facial weakness followed the injection; in one woman it lasted only a few hours, but in the other patient, a deaf mute, a complete ipsilateral paralysis of the face was present for nearly a year after the injection of only 1 cc. of alcohol. The actual injection caused no pain and produced analgesia throughout all three divisions of the trigeminal nerve. Then gradually, within a few more minutes, the weakness of the facial muscles appeared and soon became complete. Because of difficulty in communicating with this man, I omitted testing after each fraction of a cubic centimeter of alcohol was injected. Since this experience I have been careful to check the patient's sensation on the face after the injection of each additional 0.2 to 0.3 cc. of alcohol. No other undesirable sequelae occurred in any of the other patients.

INJECTION INTO THE MAXILLARY DIVISION

Inasmuch as textbooks on radiology do not give specific directions for demonstration of the foramen rotundum, the method of so doing is described herewith. The patient lies prone, as shown in figure 4, in such fashion that Reid's base line, joining the middle of the external auditory meatus with the floor of the orbit, makes an angle of 20 to 25 degrees with the vertical plane in which the radiation is directed, so that the external auditory meatus is caudal to the central ray. The long axis of the nerve is then parallel to the radiation, and the foramen rotundum, at a right angle

Fig. 6.—The foramen rotundum stand out sharply just medial to the point of the needle.

to it, will usually show up clearly. Figure 5 shows a skull in which small wires have been placed in each foramen rotundum and a projection taken as described. Figure 6 shows the radiographic procedure at the time of injection.

This projection is useful whenever clinical sensory loss in the maxillary division makes one suspect a neo-

plasm here. In 2 such cases of mine the roentgenograms showed gross enlargement of the foramen rotundum, which led to subsequent verification of the diagnosis of tumor at that point.

The procedure for insertion of the needle is in general the same as that for the injection into the mandibular division except that the needle point is inserted 3 cm. anterior to the posterior bony margin of the condyle of the mandible and is directed with the point forward at an angle of 100 to 115 degrees to the sagittal plane of the zygoma. The point is also directed upward at an angle of 100 to 130 degrees to the line in the coronal plane joining the side of the skull to the zygoma. The narrow cleft of the pterygomaxillary fissure between the maxilla anteriorly and the lateral pterygoid plate posteriorly is found with the needle, the point of which is then thrust into the pterygopalatine fossa. A series of roentgenograms and replacements of the needle follow until the point is in the proper position. From 1.5 to 4.0 cc. of 90 per cent alcohol is then injected until thorough analgesia throughout the area of the second division is obtained.

COMMENT

In only 2 patients was there failure to refer pain to the side of the nose, cheek, upper lip, upper gum or hard palate when the needle was correctly placed. In all the patients in whom a specific note was made, pain was referred to one or more of these areas when the injection of alcohol was begun. Thus it would appear that a more consistent reference of pain to the autonomous zone of the maxillary division occurs than is the case with the mandibular division. The 19 cases handled in this way included patients in whom a severe hypalgesia or analgesia was already present before the injection and patients with major facial deformities as well as those in whom a previous trial without roentgen control had failed. In each of the 19 cases all or nearly all of the upper lip and gum, medial portion of the cheek, lower part of the nose and hard palate were rendered analgesic to pinprick. The depth of the foramen varied from 4.2 to 5.8 cm. in the female patients and from 4.8 to 6.3 cm. in the male patients.

No attempt was made to cause the alcohol to travel backward to the ganglion by pointing the bevel of the needle posteriorly, because of the long distance back to the nerve cells. Corresponding to this lack of destruction of the cells was the relatively short duration of freedom from pain, averaging only seven months in the patients with trigeminal neuralgia.

SUMMARY

Methods for the injection of alcohol into the second and the third divisions of the trigeminal nerve, involving radiographs to ascertain the position of the needle, are described. The advantages of these methods are: the pain of the procedure is decreased; the number of complete injections into the nerve is increased to over 95 per cent of those attempted, and the average duration of relief from the pain of trigeminal neuralgia following injections into the third division is increased to at least thirty months. One accomplishes this by pointing the bevel of the needle upward and allowing the alcohol to penetrate up the nerve trunk to the cells of the gasserian ganglion.

MEDIAL EPICONDYLE INJURIES

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Separation of the epiphysis of the medial (internal) epicondyle (epitrochlea) of the humerus is, as the name implies, an injury of childhood or adolescence. Its occurrence is more frequent than is usually supposed. It may occur in conjunction with a dislocation of the elbow joint, or it may occur alone. The general consensus that this is an injury of serious magnitude would seem to depend on the following reasons: 1. Since a growing portion of the bone is injured, there must therefore result a high proportion of growth disturbance, with its accompanying deformity and disability. 2. Unless nearly perfect reduction of the displaced epicondyle fragment is obtained with closed or open reduction, there will occur a likelihood of fibrous union rather than bony union, with resulting pain and disability. 3. Uncorrected distal displacement of the epicondyle will lead to weakness of the flexor muscles of the wrist. 4. Ulnar nerve disturbance will occur as a result of displacement and irritation by the fractured surface of the epicondyle, by encirclement with scar tissue or by growth disturbance and irregularity of the epicondyle.

TABLE 1.—*Epiphyseal Ossification Centers in Region of Elbow (As Seen on Roentgen Examination)*

	Age at Which Epiphyseal Ossification Centers Appear (Years)	Age at Which Epiphyseal Ossification Centers Unite with Shaft (Years)
Capitellum (and outer part of trochlea)..	2	16
Trochlea (inner part).....	11	
Medial epicondyle	5	18
Lateral ep.condyle	13	16
Olecranon	10	16
Radial head	5 to 7	16 to 20

I cannot agree with these conclusions, and I will endeavor to show not only that many of these injuries are trivial but that late complications and poor functional results often occur because of overtreatment and too much conservatism. One must not overlook the fact that certain injuries to the medial epicondyle, such as complete avulsion from the humerus with displacement into the elbow joint or traumatization of the ulnar nerve at the time of the original injury, are serious injuries from their inception.

The purpose of this paper is, first, to point out the frequency of injury to the medial epicondyle, the variations of the injury and displacement, its associated lesions and complications, treatment of the injury and what may be done to minimize or correct any possible late complications. Second, this paper will deal with an analysis of 143 cases of patients with this injury who were treated in the Presbyterian Hospital, New York City, during a fifteen year period and followed sufficiently long to permit the drawing of conclusions as to the advisability of the treatment employed. I shall also dispel some of the aforementioned misconceptions.

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Read before the Section on Orthopedic Surgery at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1949.

INCIDENCE

Of all the fractures involving the lower extremity of the humerus, separation of the epiphysis of the medial (internal) epicondyle ranks second only to the supracondylar fracture in frequency.

ANATOMY

The lower extremity of the humerus is broadened to form two condyles, the most distal portions of which are shaped to form the articular surfaces of the trochlea and capitellum. Surmounting each condyle is an epicondyle, the medial giving rise to the site of origin of the flexor-pronator group of muscles and the lateral forming the site of origin of the extensors of the wrist. In childhood the capitellum, trochlea and lateral and medial epicondyles are each made up of a separate ossification center. Roentgen examination shows that these appear at different ages, increase in size and eventually join with the diaphysis at different ages. The appearance of each and its eventual union is often confusing to the student or to the physician who has but infrequent opportunity to see or treat injuries in the region of the elbow. Table I illustrates the variations met at any age. An allowance of one year (or perhaps two years) should be made in the extremes of this table, since these figures are rough averages and there is considerable variation due to racial characteristics.

The medial (internal) epicondyle epiphysis is really not an epiphysis but an apophysis. It does not in itself enter into the formation of the articular surface of the joint. It is similar to the greater and lesser trochanters in that it projects from the bone as a muscle and ligamentous attachment only. If injured or detached and separated from its base, it frequently shows subsequent disturbance in its growth, such as undue enlargement or irregularity. Moreover, when it becomes reattached to the humerus after a separation, it is more common for this attachment to be by fibrous rather than by bony union.

MECHANISM OF INJURY

The mechanism by which the medial epicondyle epiphysis is separated is not always clear, but in all probability it is similar to that which causes a posterior dislocation of the radius and ulna on the humerus, namely, a fall on the hand with the elbow in extension. Supination of the forearm, extension of the wrist and hand and any force that tends to abduct the forearm bones on the humerus at the elbow would obviously increase tension on the flexor-pronator group of muscles and through these on the epicondyle itself. This mechanism and increased tension cause the epiphysis to be avulsed from the condyle. There are, of course, different degrees of displacement, depending on the amount of force applied and on how long this force is allowed to act. These injuries are true fractures, with the fracture line passing through epiphyseal cartilage rather than through bone.

CLASSIFICATION OF INJURY

There are five various types of injury to the medial epicondyle: (1) epiphyseal trauma without separation roentgenographically visible, (2) slight separation of the epicondyle, (3) definite separation of the epicondyle, with or without dislocation of the elbow joint, (4) definite separation of the epicondyle, with displacement into the elbow joint, and (5) fracture of the medial epicondyle in adults.

CARE OF THE INJURY

Epiphyseal Trauma Without Separation.—Diagnosis: A history of a fall on the hand, followed by pain on the medial aspect of the elbow and tenderness in the region of the medial epicondyle, with or without swelling but without bony deformity, and a normal roentgenogram of the injured as compared with the uninjured elbow are strongly indicative of epiphyseal trauma without separation. The pain is usually increased by attempts of the patient to pronate this forearm against resistance. No abnormal ulnar nerve signs should be present unless the patient has sustained a direct contusion, which is rare at this site.

Treatment: No splint is necessary in the treatment of this condition. The use of a sling is advisable to allow partial rest and relaxation of the flexor muscles of the wrist. Mild active motion in the sling and soaks in warm water three times a day are beneficial to the circulation and help to decrease swelling and pain. Pain and tenderness should disappear entirely in two to three weeks, and the disability should last no longer or little longer.

Fig. 1.—Separation of the medial epicondyle epiphysis, with slight displacement.

Slight Separation of the Epicondyle.—Diagnosis: Slight separation of the epicondyle is manifested by the same pain and tenderness felt in epiphyseal trauma without separation. In addition, swelling is likely to be greater. The medial epicondyle may be slightly movable and may occasionally give crepitus on palpation. Roentgen examination will confirm the diagnosis and will rule out or disclose additional bony injuries (fig. 1). Ulnar nerve signs (motor and sensory) should be looked for or ruled out.

Treatment: Treatment consists of complete rest, with the arm and forearm in a posterior molded plaster of paris splint and sling for four or five days and with the elbow flexed at a right angle and the forearm in midrotation. The plaster splint should extend from the axilla to the metacarpophalangeal joints. After removal of the splint the patient should wear a sling for another one to two weeks, during which time he should remove it every hour or two during the day to exercise the

elbow for five to ten minutes, with special stress on regaining extension. This latter motion is particularly slow in returning, and it may take the patient as long as a year to recover it completely if the elbow has been kept fully immobilized in flexion for two or three weeks. Mild active use within pain limits may be permitted safely as soon as active motion is being carried out well.

Definite Separation of the Epicondyle, With or Without Dislocation at the Elbow Joint.—Diagnosis: In definite separation of the epicondyle there is the same pain and tenderness felt as there is in both epiphyseal trauma and slight separation of the epicondyle. There is greater swelling and possible ecchymosis (rarely found in early cases). The epicondyle is missing from its usual position (but swelling may mask palpation) and is found displaced distally and freely movable in an early case. If the radius and ulna are dislocated as well, the absence of the prominence of the epicondyle in its usual position is more readily detected on clinical examination. If there is an associated dislocation of

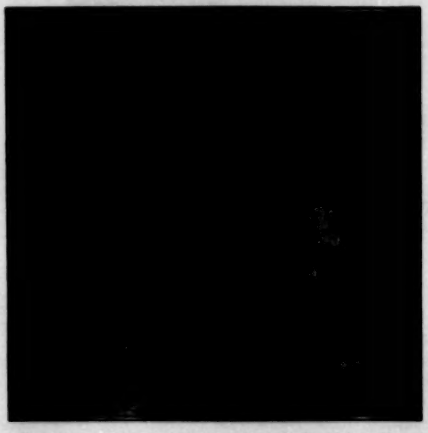

Fig. 2.—*A*, moderate displacement of the epiphysis of the medial epicondyle. *B*, same patient five years after the original injury. This patient, on last follow-up examination, had an enlarged medial epicondyle, distally displaced but nontender and nonpainful. Ranges of motion in the elbow joint was complete. Strength was full. There were no abnormal ulnar nerve signs or symptoms. The progressive development and ossification of this displaced epiphysis over a period of five years may be noted.

the forearm bones, there will be the usual deformity of this lesion. Anteroposterior and lateral roentgenograms will show both the separation of the epicondyle from the diaphysis and the amount and position of its displacement (fig. 2). These points should be checked carefully to rule out displacement of the epicondyle into the elbow joint.

Treatment: Reduction of the epicondyle is rarely possible by closed manipulation, and maintenance of reduction by external means is practically impossible. As long as ulnar nerve signs are not present or do not appear within the first two weeks after injury, there is no necessity for the performance of open reduction. It is only when the nerve is affected or the epiphysis is displaced into the elbow joint that the displacement is important (see the following paragraph). A displaced epiphysis will become healed to the medial collateral ligament of the elbow joint by fibrous union, and its displacement as much as 2 cm. distad should cause no appreciable weakness in the flexor-pronator group of muscles. Immobilization in a posterior molded splint for one week, followed by the use of a sling, active exercises and mild active use, should be sufficient treatment and a wise course to follow. (Too prolonged

Fig. 3.—Anteroposterior and lateral roentgenograms showing displacement of the medial epicondyle epiphysis into the elbow joint.

immobilization, that is three to four weeks in a plaster splint, will almost certainly delay functional return, if it does not permanently impair it.) Dislocation of the radius and ulna, if present, must be reduced by gentle traction and manipulation, but this should not alter the previously described after-treatment of the epicondyle.

Definite Separation of the Epicondyle with Displacement into the Elbow Joint.—Diagnosis: From a clinical standpoint, the diagnosis of definite separation of the epicondyle with displacement into the elbow joint may be established in the same way as that of separation without dislocation at the elbow joint, depending on the

Fig. 4.—Lateral and anteroposterior roentgenograms of the elbow, showing displacement of the epiphysis of the medial epicondyle into the dislocated elbow joint.

presence or absence of dislocation of the radius and ulna on the humerus. Roentgen examination is necessary to confirm displacement of the epicondyle into the joint (figs. 3 and 4). It may also be necessary to examine the normal elbow by roentgenogram for comparison and

positive proof. Many of these patients have already had an elbow dislocation reduced by a friend who has applied traction immediately after injury in order to overcome the deformity. The lack of obvious dislocation is sometimes misleading. The most important part of the diagnosis, aside from comparative roentgen examination of the uninjured as well as the injured elbow, is that the physician be aware that such displacement into the joint can occur and that he never be satisfied that the bony anatomy of the elbow is unaltered until all epiphyseal ossification centers are found to be in their normal positions. Careful examination for ulnar nerve function is extremely important.

Treatment: Operative procedures are preferable to manipulation when the epicondyle is displaced into the elbow joint. To attempt its removal from the joint by manipulation is rarely, if ever, successful and carries with it a likelihood of traumatism of the ulnar nerve. The belief that active motion of the elbow might squeeze the fragment out of the joint cavity is a mistaken one. Such action would later necessitate operative removal at an unfavorable time, after healing had begun.[1]

A few cases have been cited of successful attempts at manipulation to remove the fragment from the joint, but there seems to be considerable risk accompanying such a procedure.

Operative Technic: The most favorable time for operative procedures is within the first one to two days after injury. The elbow joint should be explored through a medial incision, and the wound margins should be blocked off by towels clipped to the skin. On exposure of the elbow joint, the upper portion of the flexor-pronator group of muscles will be readily identified by the glistening, white fibers of fascia over-lying them. These converge and curl laterally into the joint immediately distal to the trochlear process. The epicondyle fragment will not be seen until the forearm is abducted slightly at the elbow and these muscles are pulled out of the joint by an elevator or forceps. The epicondyle will then be thrust into full view. If there is an associated dislocation of the elbow joint, this should at this time be reduced by gentle traction and manipulation. The joint should then be flexed and extended to make certain that there is no further tendency for the forearm bones to become redislocated. The epicondyle fragment, with the attached muscles, may be replaced and fastened with a heavy silk suture passed through a drill hole in the medial humeral condyle. A nail or a wire suture may be used, if preferred. Some surgeons prefer to excise the epiphyseal fragment and merely reattach the common tendon of origin of these muscles to the humerus by means of a silk or wire suture. There is some evidence to show that complete functional return may be hastened by this latter method, but either method gives excellent results, provided active elbow motion is started no later than a week or ten days after operation.

If the ulnar nerve has been affected or if, on inspection, it appears contused, it should be transposed to the anterior surface of the reattached muscles and humeral condyle in order to relax it and prevent its becoming caught in scar tissue. Contusion of this nerve is evidenced by swelling and hemorrhage within its substance and should receive additional prophylactic treatment by the injection of isotonic sodium chloride solution into its sheath. This is for the purpose of distending it and separating its fibers to prevent fibrosis within the sheath and to hasten recovery of nerve function.

A more detailed study of definite separation of the epicondyle with displacement into the elbow joint, based on 21 cases, was published by me in 1946.

Fracture of the Medial Epicondyle in Adults.—Fracture of the medial epicondyle in adults is an extremely rare injury and usually occurs in conjunction with other fractures into the elbow joint. When it occurs alone as an isolated injury, it is usually the result of direct contusion.

The diagnosis and treatment would be similar to that of a fracture in an older child, depending on the amount of displacement. Conservative treatment followed by early active motion should result in good function. No operative procedures should be performed unless there exists evidence of ulnar nerve trauma.

ANALYSIS OF CASES

I have undertaken to review the cases of medial epicondyle injury (143 in all) treated on the Fracture Service of the Presbyterian Hospital in New York City from 1931 to 1945, inclusive, in order to acquire a better understanding of the injury and to improve the methods of treatment. One hundred and thirty-seven of these patients were children whose ages varied from 4 to 17 years, with the majority between 9 and 14 years (table 2). An injury to the medial epicondyle is a great rarity in the adult, as is shown by the fact that but 6 patients were found who sustained this injury in adult life. Still more rare in the adult is this injury unassociated with fracture of the radial head or dislocation of the elbow joint. Only 1 such case of pure medial epicondyle fracture was found, and this was caused by a direct blow with a blunt object.

TABLE 2.—*Medial Epicondyle Injuries* *

	Age Incidence												
Age (years).....	5	6	7	8	9	10	11	12	13	14	15	16	17
No. of cases.....	2	2	6	7	21	23	30	15	15	15	9	6	6

* Total number of cases, 137; 99 patients were 9 to 14 years; average age, 11.3 years.

Among the 137 children with this injury, 21 with intra-articular displacement of the epicondyle have been previously reported. This, therefore, leaves 116 patients with the injury, children without intra-articular displacement, treated in this fifteen year period.

The injury occurred, in this series, approximately four times as frequently in boys as in girls, there being 92 and 24 cases, respectively, in each sex.

Dislocation of both forearm bones at the elbow joint was associated with the medial epicondyle injury in 32 patients, or in 27.5 per cent of the cases of epicondyle injury in which the epicondyle had not become displaced into the joint. In 13 patients these dislocations had been reduced prior to the patient's admission to the Presbyterian Hospital, and the longest elapsed time following such reduction elsewhere was eleven days. In the remainder of the cases, the fractures were reduced here as part of the treatment. All of

1. Patrick, J.: Fracture of the Medical Epicondyle with Displacement into the Elbow Joint, J. Bone & Joint Surg. **28**:143, 1946. Schmier, A. A.: Fracture-Dislocation of the Elbow with Ulnar Nerve Involvement, J. Bone & Joint Surg. **18**:1030, 1936; Fracture-Dislocation of the Elbow with Displacement of the Internal Epicondyle into the Joint, Am. J. Surg. **45**:116, 1939; The Internal Epicondyle Epiphysis and Elbow Injuries, Surg., Gynec. & Obst. **80**:416, 1945.

these patients came to the clinic within a few minutes or a few hours after injury.

Associated injuries aside from dislocation of the elbow joint occurred as follows: radial head fracture (3 cases); supracondylar fracture (4 cases, 1 old); fracture of the olecranon (2 cases); fracture of the nose (1 case), and ulnar nerve contusion (1 case). Two of these patients had sustained injury to the same medial epicondyle on a previous occasion. In another myositis ossificans of the brachialis anticus muscle had developed following a previous injury treated with passive stretching.

The patients in general have been treated in the Presbyterian Hospital clinic according to the particular type of injury and degree of displacement described in the paragraph on care of the injury in the first part of this article. In only 8 patients was an attempt made to reduce the displaced medial epicondyle fragment (exclusive of those displaced into the elbow joint). In 2 patients operative replacement was performed six and fourteen days, respectively, after injury; however, this procedure would now be considered unnecessary, unjustifiable and meddlesome surgical intervention. A third patient came to the clinic, seven months after injury and four months after open reduction was performed at another hospital, with a sinus tract resulting from insertion of a wire loop for internal fixation. Treatment consisted of removal of the wire loop, which, as an infected foreign body, kept the sinus tract open. A regimen of active exercises and use was instituted, but the patient regained little extra joint motion. There were 10 other late cases, in which the patients applied at the clinic for treatment longer than two weeks after injury. These patients had been treated before coming to the clinic by plaster and sling immobilization and were subsequently treated with exercises and encouragement to use the elbow.

TABLE 3.—*Medial Epicondyle Fracture (Separation)*

Total no. of cases		143
Adults only		—6
Total no. of cases in children		137
Cases complicated by displacement of epicondyle into elbow joint (see previous report)		—21
		116
Cases with unsatisfactory follow-up		—17
Total no. of cases of satisfactorily followed uncomplicated medial epicondyle fracture		99

FOLLOW-UP RESULTS

In only 3 of the 11 late cases were completely excellent results obtained. All the remaining patients were found to have mild enlargement or prominence of the medial epicondyle or some loss of extension. The patient on whom open reduction, with wire loop fixation, was performed three months after injury and who finally came to the clinic seven months after injury, demonstrated a permanent loss of elbow extension of 50 degrees.

There were 116 cases of uncomplicated fracture of the medial epicondyle of the humerus. Of these patients, treated by my associates and me, 17 have been followed for too short a period or lost, so that these cases are unsatisfactory for analysis. Four of these patients showed excellent results when last observed, from one and one-half to four weeks after injury; 4 showed good results when last seen, from one and one-half to eight weeks after injury; 5 patients received emergency treatment only and subsequently consulted their own physicians for further care; 4 never returned after the initial visit, so the results in these cases are unknown. No late results are known in any of these 17 cases, so they are omitted from the analysis of the series. This leaves 99 cases adequately followed and considered satisfactory for analysis (table 3). Many of these patients have been checked and rechecked in our follow-up clinic with roentgen and clinical examination for results as late as seven years after the original injury. Several patients have been followed nine to ten years. (The most recently treated patients, of course, are an exception to this.)

The late follow-up results for this injury have in the vast majority been good to excellent. On the basis of actual figures, in 47 of the 99 followed patients completely perfect results, from the standpoint of lack of deformity, full and painless function and full use, were obtained. Of the remaining 52 patients, 47 may be considered to have had good to excellent results. This, therefore, amounts to 95 per cent of all the followed uncomplicated cases of medial epicondyle injury in which an ultimate clinical result that is either good to excellent or perfect has been obtained. Had the follow-up examination not been so rigid and had the injured arm not been compared to the normal arm, many of these patients might have passed as showing perfect results. The greatest functional impairment of the elbow in any of the cases was a loss of 5 to 10 degrees of full extension, which occurred in 20 cases. There were 46 patients who showed a visible or palpable abnormality in the anatomy of the medial epicondyle. This abnormality was described by one of the following terms: thickened, broadened, enlarged, prominent, lower than normal and, in 1 case, movable. The only other anatomic deformity noted has been a change of slight degree in the carrying angle. Four patients showed slight decrease and 2 showed slight increase in this angle. None of these patients demonstrated any loss of joint function. It is difficult to explain the late changes in the carrying angle, but they may be due to slight growth disturbances following injury to the entire lower humeral epiphysis which originally had passed unrecognized.

There were 5 cases in which the late functional result has been considered no better than fair. It would seem more advantageous to analyze each of these closely to determine the reasons for failure in securing a good result than it would to attempt to find the reasons for success in the cases with good results. These cases in which the results were only fair are described briefly and outlined in table 4. Four of these patients showed a permanent loss of elbow extension varying from 20 to 50 degrees. Two with lesser amounts of extension loss also had 10 degrees limitation of flexion. One patient had a permanent limitation of flexion of 40 degrees. This my associates and I believe to be the result of his elbow having been splinted in full extension for eleven days after the dislocation was reduced at another hospital. Three patients with limited extension had been treated in the clinic by weight carrying. We now consider this form of treatment to be a definite mistake. It creates muscle spasm and a protective attitude in the patient which is extremely difficult to rectify. Two of the patients with limited elbow extension required

surgical intervention. One had open reduction of the epicondyle carried out by us on the sixth day after injury; the other was the patient who had open reduction performed elsewhere three months after injury. Permanent impairment of extension of the elbow of 25 and 50 degrees, respectively, resulted in these 2 patients (table 4).

It may thus be deduced that certain combinations of pathologic conditions, elapsed time and treatment are detrimental to full functional recovery of the elbow joint following this injury. Such combinations are: an original joint dislocation; prolonged splinting after reduction, and such forms of physical therapy as massage and weight carrying. The other combination likewise detrimental to functional recovery is open reduction performed at a late date. All treatment factors in fresh or early cases are controllable by the surgeon. It would seem wise to splint (immobilize) the elbow for comfort only and for as short a time as possible rather than to protect it throughout healing. Active exercises within pain limits accompanied with warm soaks are beneficial. Passive motion, stretching, weight carrying and massage should be avoided at all costs.

Complete splinting for this injury, regardless of degree of displacement, should not exceed one week to ten days. It has been known for a long time that an elbow, after one of these injuries, if splinted in flexion for three to four weeks, may take close to a year to regain maximum joint extension. The same applies to recovery of flexion if the elbow has been splinted in extension.

The anatomic result cannot be controlled as function can be controlled. It is also of less importance. An irregular, thick, prominent epicondyle should make little difference to the patient, since recognition of this deformity is usually detected by careful palpation rather than by inspection. Late bony deformity of mild degree offers no impairment as such to the ultimate function of the joint (fig. 2*B*). Analysis of our follow-up results likewise discloses that the ultimate function of the elbow joint is not altered by the quality of healing of the displaced epicondyle fragment, whether this be by fibrous or by bony union.

TABLE 4.—*Analysis of Cases with Poor Follow-Up Results*

Patient	Age (Years)	Associated Joint Dislocation	Immobilization (Days)	Treatment: Massage	Treatment: Weight-Carrying	Open Reduction	Active Motion Begun (Days)	Duration of Treatment	Duration of Follow-Up	Remarks and Late Results
W. S.	12	Yes	14	Yes	Yes	No	5	3 mo.	6 years, 10 mo.	Medial epicondyle enlarged; elbow range, 30 to 135°
P. F.	17	No	1	No	Yes	6 days after injury	15	10 weeks	3 years, 5 mo.	Medial epicondyle enlarged; elbow range, 35 to 135°
A. S.	17	Yes	25	Yes	Yes	No	25	11 weeks	5 years, 10 mo.	Also treated with push-up exercises and injection of procaine hydrochloride into biceps muscle; medial epicondyle thickened; elbow range 30 to 130° after 4 years; subsequent injury (fracture of condyle); range after 5 yrs. 10 mos. 40 to 100°; ulnar nerve transplant required after 3 years
T. L.	12	No	..	....	....	3 months after injury	..	....	1 year, 10 mo.	Medial epicondyle prominent; elbow range, 40 to 130°
N.	17	Yes	11	No	No	No	11	3 weeks	1 year, 6 mo.	Elbow range 70 to 180°

Spasm developed. The patient was subsequently given an injection of procaine hydrochloride into his spastic biceps muscle to relax it. He was given too much treatment for too long a period. Excess scar tissue developed behind and around the displaced medial epicondyle, and subsequently the ulnar nerve became subjected to compression, necessitating operative neurolysis and transposition. The ultimate functional result, however, was excellent.

SUMMARY

The consensus that this injury is in general a serious one should be refuted. At the beginning of this article several reasons were given for this belief. First, although an injury to a growing portion of bone has occurred, it has been found, in analyzing this series of cases, that almost half the patients showed irregularity of the medial epicondyle on follow-up examination, but in none of these could any loss of function be directly attributed to this irregularity. Second, as for lack of perfect reduction of the displaced epicondyle, leading to fibrous union, pain and disability, none of the patients had any late pain and none had or showed any actual late disability. Lack of disability after injury is, of course, more common in children than in adults, owing to their great adaptability to minor or even major losses in joint function. Third, failure to reduce the epicondyle did not lead to any recognizable subjective or objective weakness in flexor muscle power of the wrist. Fourth, failure to obtain reduction of the epicondyle fragment did not lead to any late disturbance in the sensory or motor function of the ulnar nerve. Of the 116 patients with this injury treated by us only 1 developed late ulnar nerve disturbance. This occurred in case 55 (A.S., in table 4), in which the patient had a dislocation and was treated by splinting for twenty-five days, massage, weight carrying and push-up exercises.

CONCLUSIONS

1. Injury to the medial epicondyle of the humerus is common, but it is not usually a serious injury.

2. The most important diagnostic point to remember is the possibility of displacement of the epicondyle into the elbow joint.

3. All epiphyseal ossification centers must be discernible (as compared with the uninjured elbow, if necessary) in their normal locations by roentgen examination.

4. Treatment should be based upon the conditions present and should be instituted early. Conservative treatment is indicated in all cases except those in which intra-articular displacement of the epicondyle has occurred or in which ulnar nerve damage has taken place.

5. The physician should minimize the period of immobilization and institute early active exercises within pain limits.

6. The physician should avoid prolonged immobilization, passive stretching, weight carrying and late operative treatment.

7. The status of the ulnar nerve should be checked before treatment and frequently during treatment. The nerve should be treated if indicated.

8. The prognosis for this injury is excellent if the condition is treated early and wisely and is not overtreated.

ABSTRACT OF DISCUSSION

DR. LEONARD T. PETERSON, Washington, D. C.: The principles of treatment advocated by Dr. Smith may be summarized as symptomatic treatment. This report would indicate that, except in cases with the epicondyle in the elbow joint, the size and position of the fragment is not significant. Since this fracture is extra-articular and does not influence the growth or alinement of the extremity, it should not be overtreated. I have recommended excision of the fragment, repair of the soft tissues and early motion. In cases of avulsion of the epicondyle with loss of support for the ulnar nerve, internal fixation has appeared reasonable. While prolonged immobilization is undesirable, a period sufficient for union after open reduction should not in itself cause permanent loss of motion. Forced manipulation of the elbow fails to improve motion and is contraindicated. I agree that carrying weights does not increase extension, because the patient contracts the biceps and brachialis and does not stretch the capsule. There is less improvement with this treatment than without any treatment, and, in fact, there may be actual loss of extension. I have not performed closed reduction of a fragment displaced into the joint. Transplantation of the ulnar nerve is often advised, but it is difficult to find authentic cases of late neuritis due to this injury alone. Late neuritis due to combined injuries or to cubitus valgus following condylar fracture may be responsible for this teaching. Anterior transposition of the ulnar nerve is undesirable unless necessary, and this is rarely the case. If the nerve is still supported by the remaining portion of the epicondyle, it should be left alone. A contused nerve will gain maximum recovery without injections of isotonic sodium chloride, and therefore I advise minimum interference. In only 1 case in the report did ulnar neuritis develop and that was attributed to overtreatment in a case in which the patient had a displaced epicondyle. I should like to ask Dr. Smith if the presence of a displaced fragment not in the joint caused any local discomfort necessitating late removal.

DR. MAURICE M. PIKE, Hartford, Conn.: I agree with Dr. Smith's maxim of early treatment and early active motion for best functional results. I should like to discuss the possible late complications associated with this type of injury long after all epiphyseal centers are closed. This group of cases is confined entirely to the fifteen year period from 1931 to 1945, which means that in a high percentage of the cases reviewed as end results, the patients are still in the actively growing stage. Three physicians on our Hartford Hospital Staff who had serious injuries of the left elbow in childhood now, at age 50 to 55, have obvious deformities. The fathers of two of these doctors were also physicians, so that it must be assumed that the best possible medical care of the time and locality was available. One lived in Connecticut, one in New York and one in Ohio, so it can be seen that this is a widespread condition. It is to be hoped that the majority of Dr. Smith's reported patients will, after growth has ceased, continue to have good cosmetic, as well as functional, results, so that they will not be constant reminders to the orthopedic surgeons with whom they may be in daily contact in the future of a frequently embarrassing condition.

DR. WALTER P. BLOUNT, Milwaukee: Dr. Smith has presented several controversial points. He has discussed the treatment of fractures about the elbow in children and in adults. Many of the procedures outlined by him are not desirable in children. In particular, it is wrong to institute physical therapy and to manipulate the elbow passively in children. Small children are guided by instinct, almost like animals. After the bone is solid, the best result in an elbow fracture in a child is obtained by permitting the child to use the elbow only as he wishes. Forceful manipulation prolongs the recovery. I regret the inclusion of 4 adult cases. It is not clear to me whether or not the study of end results includes the adults. I should like to emphasize that fractures in children are different from those in adults.

DR. HAROLD R. BOHLMAN, Baltimore: Some years ago my associates and I reviewed our cases after twenty-five years. If the reduction of a fracture is not accurate and well healed, the fragments may have to be removed later because of local symptoms and deformities, which occur when the fragments are not accurately reduced. Accurate, early open reduction is warranted, with a sufficient period of immobilization in children to allow perfect healing. I agree thoroughly with Dr. Blount that function returns spontaneously and normally.

DR. FREDERICK M. SMITH, New York: In answer to Dr. Peterson's query about the number of patients who had displacements that were followed by ulnar nerve signs or symptoms, more than 50 per cent of the cases in our series were of children with displaced medial epicondyles, but no late ulnar nerve signs or symptoms developed in any of these cases. The series I presented did not include all the associated fractures. We have tried to analyze pure medial epicondyle injuries only, omitting all the other types of fracture which may be found with such injuries. I probably did not make clear that the actual analysis of the follow-up results in these medial epicondyle injuries was based on children's injuries only. I deducted the adult cases in the analysis and mentioned them solely to show how scarce they are and that they required little treatment. As far as ulnar nerve palsies following medial epicondyle injuries are concerned; we have not discovered any that have occurred at a late date. In the only patients we have found in whom ulnar symptoms have developed in later life, these symptoms developed from an increased carrying angle. This increased angle, which places an added strain on the ulnar nerve, occurred after fracture of the lateral humeral condyle in childhood. Ulnar nerve signs developed in these patients as late as at age 33. We have seen one patient that age, with ulnar nerve signs following original injury.

Bacitracin.—The antibiotic bacitracin is produced by the Tracey I strain of Bacillus subtilis which was discovered in June 1943 in the Laboratory of Bacteriological Research of the Department of Surgery, College of Physicians and Surgeons, Columbia University. The organism was recovered from the damaged tissue and street dirt debrided from the compound fracture of a seven year old child by the name of Tracey. The antibiotic was therefore named "bacitracin". . . . It is not toxic when given by mouth and is not readily absorbed. Some of the patients treated intramuscularly with bacitracin showed disturbing symptoms and signs of kidney irritation. Bacitracin is retained in the alimentary tract and acts on many of the intestinal bacterial species. There is evidence of a synergistic action between penicillin and bacitracin in the control of infections. Chemical studies are being pursued in an effort to purify this drug further, to identify the active principle and to separate it if possible from the toxic factor.—Frank L. Meleney and Balbina A. Johnson, New York, Bacitracin, *The American Journal of Medicine*, December 1949.

NEOSTIGMINE THERAPY IN CEREBRAL PALSY

A Critical Evaluation

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Cerebral palsy, in its moderate and severe forms, is a chronic, disabling disease whose management involves long and arduous programs of therapy. Improvement is slow and the rate of progress often discouraging. Any drug that would facilitate the rate of improvement or enhance the efficacy of a training program would be a most welcome and valuable adjutant to therapy.

It should be emphasized at the outset that a drug can never be a substitute for training in this condition but at best can afford a degree of relaxation or relief of tension that might in some way result in greater benefits and more rapid results from other forms of therapy.

Many drugs have been employed in the treatment of cerebral palsy. These include the sedative drugs, such as phenobarbital and alcohol, the antiepileptic drugs, such as diphenylhydantoin (dilantin®) and trimethadione (tridione®), drugs of the nightshade family, such as scopolamine and stramonium, and the muscle-relaxing drugs, such as curare, neostigmine and mephenesin. Of these, the nightshade group of drugs, alcohol, trimethadione and neostigmine have been reported as giving the most consistent beneficial results. We report herein our observations of the effect of this last-named drug, neostigmine, in 60 patients with cerebral palsy.

PREVIOUS CLINICAL REPORTS

Neostigmine methylsulfate[4] was first used clinically to stimulate the peristalsis of the intestinal tract and to overcome postoperative intestinal atony. An even more striking clinical effect was its amelioration of symptoms of myasthenia gravis. This led to the trial of neostigmine in a wide variety of neuromuscular disorders.

Kabat and Knapp[1] reported that in subacute and chronic poliomyelitis the administration of neostigmine caused relaxation of muscle spasm, relief from pain, increase in strength and improvement in muscular coordination. Fox and Spankus[2] found that in acute poliomyelitis neither appreciable nor consistent relaxation was produced by neostigmine therapy.

Electromyographic studies by Watkins and Brazier[3] revealed a "decrease in potentials" following injection of neostigmine in patients with muscle spasm due to poliomyelitis.

Trommer and Cohen[4] reported relief of pain and muscle spasm in rheumatoid arthritis with neostigmine therapy. Kabat[5] found the drug of value in hemiplegia, facial paralysis, fibrositis, post-fracture disabilities and subacromial bursitis.

Kabat and Jones[6] and Schaubel[7] reported excellent results in the treatment of various forms of spastic cerebral paralysis with neostigmine. Jepson[8] corroborated these observations in children with infantile cerebral paralysis who were under 12 years of age, although Pohl[9] was not able to reduplicate the results.

Thus it is evident that there have been conflicting opinions on the value of neostigmine in cerebral palsy and in other conditions characterized by muscle spasm.

PHYSIOLOGY AND PHARMACOLOGY

Neostigmine is a synthetic drug whose pharmacologic effect is similar to that of the natural alkaloid physostigmine. In addition to its parasympathomimetic action, it is also reported that neostigmine acts on the myoneural junction, on various spinal centers and, possibly, on centers in the medulla and cerebrum.

Neostigmine inhibits the formation or action of the enzyme cholinesterase, permitting the accumulation of acetylcholine at the myoneural junction and synapses throughout the body. The action of neostigmine of increasing the rate of transmission of impulses at the myoneural junction is accepted as the basis for its therapeutic effect in myasthenia gravis. By analogy, one might be led to conclude that in cerebral palsy this action would serve to increase rather than diminish muscle tonus. However, if one assumes that action of the drug on the internuncial cells[10] in the cord increases the transmission of inhibitory impulses, the relaxing action in cerebral palsy can be explained.

MATERIALS AND METHODS

After publication of the original reports on the beneficial effects of neostigmine in cerebral palsy, we began to use the drug in selected cases. After the appearance of a report in a popular magazine acclaiming the almost miraculous benefits from neostigmine in cases of cerebral palsy, pressure of patient demand for the use of the drug became so great that for a while it was difficult to obtain on the market. At the same time, we noted a decided increase in the reports of our patients of the benefits that they were apparently deriving from the drug. Frequently the reported benefits were so rapid and dramatic as to suggest that psychologic factors might have played at least some role in this improvement.

Accordingly, it was decided to make a careful and controlled study in order to evaluate the actual role played by the drug.

Sixty patients with moderately severe to severe degrees of cerebral palsy of various types were selected for treatment with neostigmine. They were observed and treated in private practice, in an outpatient therapeutic nursery, in a neurology outpatient clinic and in an inpatient hospital school. In every instance the

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From Michael Reese and Cook County hospitals, Chicago, and St. John's Home and Hospital for Crippled Children, Springfield, Ill.

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patient was given as intensive a program of physical, occupational and speech therapy as his condition and our facilities permitted, before, during and after the trial with neostigmine therapy. A closely supervised program devised to foster the maximum personality development and to provide regular as well as special educational methods was in effect in the therapeutic nursery and the hospital school. Braces and other mechanical aids were employed where indicated. Anticonvulsive and pediatric care were included in a complete program of general medical care.

Only mentally educable patients were included in this study, and all patients had been under observation and treatment for months to years before neostigmine medication.

After our initial examination of the patient use of drugs other than those prescribed was not permitted.

TABLE 1.—*Summary of Results of Neostigmine Therapy During Ten Week Trial Period in Cases of Spastic Paralysis*

Case	Age in Yrs.	Involvement	Number of Days of Neostigmine Therapy	Dosage in Mg. T.I.D.	Benefits Directly Attributable to Neostigmine
1	3	Hemi.	30	7.5 to 15	None
2	4	Quad.	30	7.5 to 15	None
3	5	Quad.	135	7.5 to 15	None
4	6	Quad.	30	7.5 to 15	None
5	6	Para.	30	15 to 30	None
6	6	Para.	180	7.5 to 15	None; some regression
7	6	Hemi.	30	7.5 to 15	None
8	7	Quad.	30	10	None; some regression
9	7	Hemi.	75	15 to 30	None; some regression
10	8	Para.	45	15 to 30	None
11	8	Quad.	90	15 to 30	None
12	8	Hemi.	165	15 to 30	Slight benefit; less tension; improvement in hand function
13	8	Quad.	90	15 to 30	None
14	9	Quad.	210	15 to 30 plus 1 cc. 1:2,000*	None
15	9	Quad.	60	15 to 30	None
16	10	Quad.	180	30	None; some regression
17	11	Para.	30	15 to 30	None
18	14	Quad.	60	15 to 30	None
19	15	Quad.	45	15 to 45	Definite improvement: better speech, balance and locomotion
20	20	Quad.	180	30 to 45	Questionable improvement in speech and tension
21	22	Hemi.	42	30	None
22	30	Para.	35	30 to 45	None

* Hypodermically given neostigmine methylsulfate.

These were provided by the physician, the nursery or the school, and the bottles were unlabeled except for instructions and code numbers; all drugs prescribed were in the form of capsules or tablets of identical appearance. Only the physician in charge knew the nature and dosage of the medication. On occasion a patient or therapeutist was told that the drug being administered was neostigmine, though it may or may not have been, in an attempt to evaluate the influence of suggestion on his appraisal of response to medication.

In general, patients were given five different preparations, each for a period of two weeks, during the initial ten week trial period. In varying sequence these were: (1) a small dose of neostigmine bromide; (2) a placebo of lactose; (3) trimethadione[11]; (4) a large dose of neostigmine bromide, with sufficient atropine sulfate to overcome undesirable side effects, and (5) atropine sulfate alone, in the same dosage as that given with neostigmine bromide.

11. Our experience with this drug will be reported in a subsequent communication.

TABLE 2.—*Summary of Results of Neostigmine Therapy During Ten Week Trial Period in Cases of Athetosis*

Case	Age in Yrs.	Number of Days of Neostigmine Therapy	Dosage in Mg. T.I.D.	Benefits Directly Attributable to Neostigmine
23	1	30	7.5	None
24	3	30	7.5 to 15	None
25	3	180	15	None
26	4	60	15	None
27	4	30	7.5 to 15	None
28	5	150	15	None
29	5	30	7.5 to 15	None
30	5½	30	7.5 to 15	None
31	6	30	7.5 to 15	None
32	6	150	15 to 30	None
33	6	30	15	None
34	7	90	15 to 30	None
35	7	30	15 to 22.5	None
36	7	210	15 plus ½ amp.* daily	None
37	8	100	15 to 30	Definite benefit: reduced tension, better speech and hand function
38	8	60	15 to 22.5	None
39	10	150	15 to 30	Definite benefit: reduced tension, better speech and hand function
40	10	270	15 to 30	None
41	10	30	15 to 30	None
42	10	30	15 to 22.5	None
43	11	180	15 to 30	None
44	12	60	15 plus ½ amp.* daily	None
45	13	60	22.5	None
46	13	100	15 plus 1 amp.* daily	None
47	15	45	15 to 30	None
48	15	210	22.5	None
49	15	30	15 to 30	None
50	17	45	30 to 45	None
51	18	120	30 plus 2 amps.* daily	None
52	19	90	30 plus 1 amp.* daily	None
53	22	60	30	Slight improvement (10%)

* The abbreviation amp. indicates an ampul of neostigmine methylsulfate; one ampul contains 0.5 mg. of the drug.

TABLE 3.—*Summary of Results of Neostigmine Therapy During Ten Week Trial Period in Cases of Rigidity, Ataxia and Dystonia*

Case	Age in Yrs.	Diagnosis	Number of Days of Neostigmine Therapy	Dosage in Mg. T.I.D.	Benefits Directly Attributable to Neostigmine
54	4	Rigidity	30	7.5	None; made worse
55	7	Rigidity	60	22.5	None
56	9	Ataxia	90	30	None
57	13	Ataxia	120	30	None
58	13	Dystonia	30	30	None
59	16	Dystonia	30	30	None
60	20	Dystonia	60	30	None

In all cases a large enough dose of neostigmine was given to produce the parasympathomimetic side effects of the drug. In general the following oral dosages of neostigmine bromide were required: for patients 1 to 6 years of age, 7.5 to 15 mg. three times a day; 6 to 12 years, 15 to 30 mg. three times a day, and 12 to 30 years, 30 to 45 mg. three times a day. In six cases the drug was given both orally and hypodermically. The hypodermic dose ranged from 0.5 to 2 cc. daily of a 1:2,000 solution of neostigmine methylsulfate.

After the initial ten week trial period the largest tolerated dose of neostigmine was usually continued for one to five months, or a second trial period, altering the sequence of the medicaments, was initiated.

Progress observations were submitted periodically by therapeutists, patients, school teachers and physicians. Functional activity graphs, achievement charts, samples of writing, graphs of speech progress and of goniometric measurements were used in order to assess progress. Such observations were recorded for a minimum of three months and an average of nine months after the termination of neostigmine medication to allow observation for such prolonged or delayed action as might occur.

vided the patient and his therapeutists were unaware of the change.

In no field of therapy was there constant or frequent improvement of even a slight degree which could be attributed to neostigmine. Some therapeutists were so convinced of the therapeutic value of the drug that they invariably reported improvement when they believed that their patient was receiving it. Older patients frequently asserted that they felt better and more relaxed while receiving neostigmine, but this subjective well-being continued when they were given placebos. Moreover, if the patient or therapeutists were told that neostigmine therapy was being stopped, regression was frequently reported even though administration of neostigmine in the same or a higher dosage was continued. Thus, of 22 patients with spasticity only 1 displayed pronounced and definite improvement attributable to the drug.

Athetosis.—Of 31 patients with tension athetosis, all with quadriplegia and varying degrees of tension, in 14 the condition was classified as moderately severe and in 17 as severe. Neostigmine bromide was administered from a minimum of 30 days to a maximum of 210 days, with an average of 90 days. Five of the patients in this group also received daily hypodermic injections of one half to 2 ampules (0.25 to 1 mg.) of a 1:2,000 dilution of neostigmine methylsulfate for 30 to 90 days (table 2).

TABLE 4.—*Record of Speech Progress in Case 4 with Various Medicaments, Showing Absence of Improvement on Drug Therapy*

Accomplishments	A Sept. 27 (Trimethadione)	B Oct. 4 (Placebo)	C Oct. 18 (Neostigmine)	D Nov. 1 (Placebo)	E Nov. 15 (No Medication)
Extension of tongue	½ inch from point at corner of lip	1 inch from point at corner of lip	Same as B	Same as B	Same as B
Extend tongue; move to left side	Slight	Slight	Slight	Slight	No movement at all
Extend tongue; move to right side	Not at all	Same as A	Same as A	Same as A	Same as A
Turn tongue tip up	Lower edge of upper teeth	Lower edge of upper lip	Same as B	Same as B	Same as B
Turn tongue tip down	1 inch down from point at corner of mouth	1¼ inches down from point at corner of mouth	Same as B	Same as B	1 inch down from point at corner of mouth
Sustain "ah" on one breath	3 seconds	8½ seconds	6 seconds	6 seconds	3 seconds
Say "mah" 10 times (lip and jaw repetitive movement)	17½ seconds	13⅝ seconds	16 seconds	10½ seconds	10½ seconds
Say "lah" 10 times (repetitive movement of tip of tongue)	13½ seconds	10½ seconds	10⅝ seconds	9½ seconds	10 seconds
Say "lag" 10 times (back of tongue repetitive movement)	10½ seconds	9⅝ seconds	9½ seconds	8½ seconds	9 seconds
Say "wah" 10 times (repetitive movement of lip and jaw)	12 seconds	10 seconds	10 seconds	9 seconds	9½ seconds

RESULTS

Spastic Paralysis.—Of 22 patients with involvement of the pyramidal tract and resultant spasticity, in 9 the process was graded moderately severe and in 12, severe. Five had hemiplegia, 5 paraplegia and 12 quadriplegia. Their ages ranged from 3 to 22 years (table 1).

Neostigmine was administered from a minimum of 30 days to a maximum of 210 days, the average being 80 days. Only one patient in this group received neostigmine hypodermically as well as orally.

In 1 patient (case 19) there was definite improvement in both speech and locomotion which might be attributed to neostigmine. A second patient (case 12) showed slight improvement with less tension and better function of the hand. In a third patient (case 20) there was equivocal improvement in speech and tension. In 16 patients there was no confirmed evidence of any type of gain. Four patients exhibited regression in their clinical symptoms while receiving the drug.

In 10 of the 22 patients in this group improvement was reported to have appeared soon after administration of the medicament was started, regardless of whether it was neostigmine or a placebo. When the initially given drug was neostigmine, the "improvement" persisted after the drug was replaced by a placebo, provided the patient and his therapeutists were unaware of the change.

In 2 patients (cases 37 and 39) neostigmine appeared to be of definite benefit, reducing tension and improving both speech and hand function. In 1 patient (case 53) slight improvement in relaxation and locomotion appeared. Twenty-seven patients did not show improvement in any field of endeavor or in relaxation which could be attributed directly to neostigmine.

The psychologic or suggestive value of drug therapy, especially neostigmine, appeared to be as prominent in the persons with athetosis as in those with spastic paralysis. Improvement in function or diminution of tension were frequently reported when it was believed that neostigmine was being administered. Such improvements were usually not substantiated by any measurable functional gains.

Ataxia, Rigidity and Dystonia.—The disease of 2 patients was classified as rigidity, of 2 as ataxia and of 3 as dystonia. Ages ranged from 4 to 20 years. Neostigmine was administered for an average of sixty days. In no case was there any apparent benefit from such therapy (table 3).

REPORT OF CASES

For purposes of brevity only 4 illustrative reports of cases will be given.

CASE 1.—*Psychologic Effect of the Drug on Patient.*—A. B., a white woman aged 22, had left spastic hemiplegia since birth. Neostigmine bromide in doses of 15 mg. three times a day was

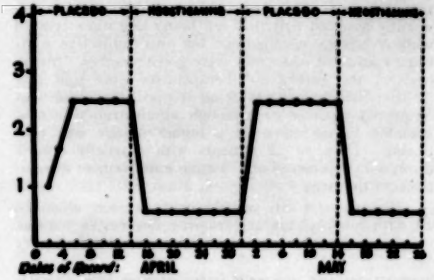

Fig. 1 (case 2).—Graphic record of the therapeutist's estimate of the effect of drugs on hand function and relaxation of patient. At the left, the numeral 4 indicates excellent relaxation and good function of the hands; estimates range downward to 0, which indicates decided tension and complete disability of the hands.

given at her own request. Twenty-four hours after the start of such therapy the patient claimed remarkable improvement: with her hand she was able to grasp and release objects more rapidly; she was able to get her heel down to the floor with greater ease; she felt more relaxed, and her working efficiency improved. Without her knowledge the neostigmine was replaced with a placebo; she continued to experience the same improvement. Within two to three hours after administration of the placebo was stopped she felt all the muscles in the left side of the body tighten, so that her left hand "curled up," and she had great difficulty in balance and walking. She has been taking this placebo for two years under the impression that

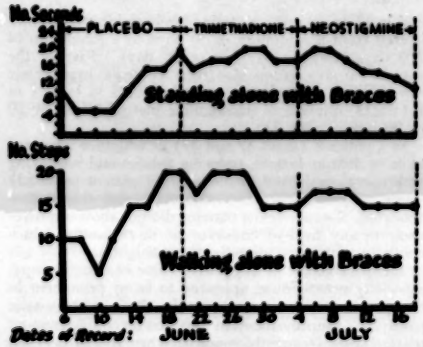

Fig. 2 (case 4).—Graphic record of standing and walking ability of the patient while various medicaments were being administered.

it is neostigmine, and she continues to experience the same improvement along with the same relapses when she misses even a single dose.

CASE 2.—*Psychologic Effect on the Therapeutist of the Use of Neostigmine by the Patient.*—C. S., a child 4 years of age, had tension athetosis. The achievement graph showed prompt improvement in this patient with medicine believed to be neostigmine. The therapeutist was informed that the medicine would be changed every two weeks, with neostigmine the initial drug. Instead, a placebo was given at the start. The therapeutist was asked to estimate the degree of relaxation and to measure functional ability in the hands of the patient. Figure 1 is a composite record of this evaluation.

CASE 3.—*Beneficial Effect Due to Atropine, Wrongly Attributed to Neostigmine.*—H. B., aged 19, with quadriplegic athetosis, was given neostigmine orally and hypodermically. The maximum daily dose was 30 mg. of neostigmine bromide given orally three times a day and two ampuls of 1:2,000

Fig. 3 (case 4).—Hand function with various medicaments as revealed by samples of patient's handwriting: *A*, after two weeks of therapy with calcium lactate placebo; *B*, after two weeks of neostigmine therapy, and *C*, after two weeks of trimethadione therapy.

solution of neostigmine methylsulfate with $\frac{1}{130}$ grain (0.4 mg.) of atropin given hypodermically once a day. The patient showed pronounced improvement while receiving such medication with loss of beneficial effects when placebos of distilled water were given, with a return of beneficial effects when the patient received placebos of distilled water containing $\frac{1}{130}$ grain (0.4 mg.) of atropine. Obviously the benefit in this instance was due to the atropine.

CASE 4.—*Graphic Methods Used to Record Progress of Patients on Drug Therapy.*—J. B., aged 9 years, had severe tension athetosis; graphic records of function of hands and

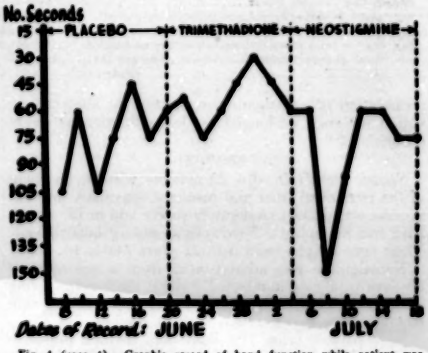

Fig. 4 (case 4).—Graphic record of hand function while patient was receiving medicaments, showing the time required to place ten objects in the "teach 'em board."

lower extremities failed to reveal any improvement while he was receiving neostigmine (figs. 2, 3 and 4; table 4). Frequent reports of improvement were not substantiated by measurable functional gains.

COMMENT

Abundant experimental and clinical evidence exists that neostigmine causes relaxation of spasticity and diminution of tonus in spastic muscles. This effect, though physiologically demonstrable, is not sufficient to benefit clinically patients with severe forms of cerebral palsy. In only 3 of our 60 cases could we find apprecia-

ble or sustained improvement in extremity function, degree of tension or speech which could be attributed directly to neostigmine therapy. In 2 other cases there was slight to moderate, and in 1 questionable, improvement. The condition of 4 patients seemed to be worse while they received neostigmine.

In over half of the 60 patients varying degrees of improvement were reported whenever the patient, parents or therapeutist believed that neostigmine was being administered. Such "improvement" would stop abruptly, and frequently regression would begin, when the drug was "changed" to a placebo, trimethadione or neostigmine of the same or larger dosage.

Reports of improvement on "neostigmine" therapy in our series of cases were especially frequent and pronounced after publication of an article in a widely read lay periodical acclaiming the value of neostigmine therapy in cerebral palsy.

Reports by patients and therapeutists of improvement while neostigmine was being administered were usually not substantiated by demonstrable functional gains which could be definitely attributed to that drug.

The greatest therapeutic gain while the patient received "neostigmine" therapy was in a feeling of optimistic well-being, and it soon became apparent that the psychologic value of the drug was of greater importance than its pharmacologic action. In several cases the suggestive effect of "neostigmine" administration was such that both patients and therapeutists were stimulated to greater efforts, with resultant gains which would continue when placebos replaced the neostigmine without their knowledge.

Follow-up observations failed to reveal any cumulative or delayed benefits which could be attributed to neostigmine.

In an attempt to reconcile our observations with those of other investigators who found neostigmine to be of such specific value in the treatment of cerebral palsy we offer the following considerations:

1. Persistent constipation, a common complaint in cerebral palsy, is relieved by neostigmine. This may afford greater relaxation and a feeling of well-being in the patient; in addition it may relieve the anxiety of the parents, thus indirectly benefiting the patient.

2. In some of the series previously reported physical, occupational and speech therapy were either initiated or increased at the time neostigmine therapy was started. It is possible that these patients might have improved with the additional general therapies even if the drug had not been given.

3. Many of these previous studies were conducted in institutions or nurseries where increased opportunity for social and educational development was afforded. With such improvement in the social and educational milieu of the patient concomitant improvement in physical condition is frequently observed without special therapies or drugs.

4. Spontaneous improvement is frequently seen in patients with severe cases of cerebral palsy and should not necessarily be attributed to any drug that is being administered simultaneously. When six to eight months ensue before improvement is noted, such improvement may well be spontaneous, as the result of natural, though delayed, innate forces. There is no clinical or pharmacologic evidence to support the concept of cumulative or delayed action of neostigmine.

5. The psychologic (suggestive) factor inherent in treatment with a drug, especially one that has received such favorable publicity, may not have been fully appreciated in previous evaluations of neostigmine therapy in cerebral palsy.

6. A large percentage of patients with cerebral palsy have associated visual and auditory defects. Improvement in speech, self help, locomotion and even psychometric performance may follow the correction of these defects by the use of glasses and hearing aids. One might easily attribute such improvements to the (simultaneous) administration of neostigmine.

7. To our knowledge no previous investigators have reported the use of adequate controls. Some investigators who previously reported favorable results in cerebral palsy with neostigmine therapy have now modified [12] or even reversed their opinions, and have stopped giving the drug in these cases.

8. Although 6 of our patients were given neostigmine hypodermically as well as orally, our investigations were primarily based on oral administration of the drug. This poses the question whether our results might have been different if neostigmine were given hypodermically or in larger oral doses. However, from the known pharmacologic and physiologic properties of neostigmine, one would expect to obtain the same results with either oral or hypodermic administration, provided the oral dose was large enough. This has been found to be true in cerebral palsy [13] as well as in myasthenia gravis. In the 6 cases in which the drug was given hypodermically as well as orally results were similar to those in patients who received only the oral dose. The foregoing reasons convince us that the route of administration of neostigmine is inconsequential as long as the dose is sufficient to give a pharmacologic effect.

9. The atropine usually given to counteract side effects of neostigmine may have been responsible for some of the improvement previously recorded. It is well known that drugs of the nightshade family may alleviate symptoms due to extrapyramidal lesions.

CONCLUSIONS

1. Definite improvement which could be attributed to the specific action of neostigmine was found in only 3 of 60 controlled cases of cerebral palsy (1 patient with spastic paralysis and 2 with athetosis). Three other patients displayed questionable or slight improvement.

2. The importance of psychologic (suggestive) factors in the administration of a popularized drug was demonstrated repeatedly throughout our investigations.

3. Inasmuch as the psychologic milieu appears to be of such importance in the treatment of cerebral palsy, it may be wise to allot a greater portion of general treatment to psychiatric therapy.

4. Improvement occurs even in patients with severe forms of cerebral palsy, both spontaneously and as a result of various therapies. The reasons for such improvement must be carefully assessed before the improvement is attributed to any single measure.

5. Neostigmine therapy has not shown sufficient specific benefit to merit routine use of the drug in any form of cerebral palsy.

12. Schaubel, H. J.: Personal communication to the authors.
13. Schaubel,[1] Jepson.[3]

Clinical Notes, Suggestions and New Instruments

STREPTOMYCIN IN THE TREATMENT OF TUBERCULOUS TENOSYNOVITIS

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The treatment of tuberculous tenosynovitis ranged from immobilization to surgical removal of the affected areas prior to the discovery of streptomycin. Since then, the drug has been used in conjunction with both forms of surgical therapy, although there is little information in the medical literature on the subject of the use of streptomycin in tuberculous tenosynovitis.

Immobilization, relative or absolute, is one of the keystones in the treatment of tuberculosis. However, splint fixation of the wrist and fingers for a prolonged period will lead to some ankylosis of these many joints, thus creating a problem in rehabilitation after the tuberculosis is controlled. Any method of treatment which does not include surgical intervention and/or immobilization and which gives good results would seem to have economic merit. An opportunity has been afforded us to treat 2 patients with tuberculous tenosynovitis with streptomycin without surgical measures or immobilization.

REPORT OF CASES

CASE 1.—A white man, aged 56, had had a swelling of the right wrist for about ten months. One month after the onset of swelling, the wrist became painful. Treatment, which was undertaken elsewhere, consisted in the application of heat and physical therapy, followed by immobilization of the wrist for five weeks without effect. Surgical operation was performed, and a diagnosis of tuberculous tenosynovitis was made. At the time of the patient's admission to the surgical service on April 19, 1949 the swelling and pain had recurred.

The physical examination revealed essentially normal conditions except in the right wrist and hand. A tumor measuring about 7 by 2.5 cm. extended from the volar surface of the wrist to the base of the fifth finger. Moderate limitation of flexion of the fourth and fifth fingers was present. Hyperesthesia and numbness were found over the volar surface of the palm and the fourth and fifth fingers.

Results of laboratory examinations were within normal limits. Sputum examinations were negative for tubercle bacilli. Roentgen examination of the thorax and right wrist was interpreted as revealing normal conditions. A diagnosis of tuberculous tenosynovitis was made.

Streptomycin, 0.5 Gm. twice a day, was given intramuscularly for six weeks. The right wrist was not immobilized. Much of the numbness was alleviated, and considerable improvement in flexion of the affected fingers was noted after four weeks of treatment. One month after the completion of therapy, appearance and function were practically normal.

The patient was seen again slightly less than one year after his first admission to our care. He stated that symptoms had again been present for about three weeks. Physical examination revealed the same condition as at the time of the first admission. A biopsy of the involved area showed scar tissue. It was considered that the patient had had a true recurrence of his tuberculous tenosynovitis despite the report of the histologist. Streptomycin was administered as in the first instance. The response to treatment was excellent. The patient was seen again slightly more than three months after discharge. The wrist was not swollen, and function of the hand was excellent.

CASE 2.—A white man, aged 35, stated that he had had a dull, aching pain in the right inguinal region about sixteen months previously. An abscess which developed there was incised, and subsequently the area healed rapidly. About eight months before admission, a tumor appeared on the anterior surface of the left wrist and grew slowly in size. Weakness of the hand and hyperesthesia of the fourth and fifth fingers developed. About three weeks before admission, a second abscess in the inguinal area was noted, and spontaneous drainage occurred.

The man was admitted to the Veterans Administration Hospital at Fort Howard Feb. 3, 1949. The physical examination revealed essentially normal conditions except in the left wrist and hand and the right groin. A soft tumor, not tender, measuring 8 by 4 cm., was present on the volar surface of the left wrist. Diminution of sensation was found over the volar surfaces of the third, fourth and fifth fingers. A sinus tract about 4 cm. long was present in the medial aspect of the right groin just inferior to the pubic tubercle.

Results of the laboratory examinations were within normal range. Sputum examination, a smear of the urinary sediment and culture of the urine were negative for tubercle bacilli. Roentgenographic examination of the thorax and left wrist and excretory urograms were normal. The roentgenogram of the pelvis revealed decided destruction of the right pubic bone in the region of the symphysis pubis. A biopsy specimen of the tumor of the left wrist was taken, and curettage of the sinus tract and right pubic bone were performed. Tissue from both sources was found to be tuberculous.

Streptomycin, 0.5 Gm. twice a day, was given for six weeks. The left wrist was not immobilized. The swelling of the left wrist and the weakness and hyperesthesia of the fourth and fifth fingers of the left hand disappeared. The sinus tract in the right pubis closed. After the completion of the administration of streptomycin, a second biopsy of the left wrist revealed healing tuberculosis.

Four months after the cessation of therapy, the patient stated that he had been working as a crane operator, using his left wrist considerably, without recurrence of symptoms. The left wrist was practically normal in appearance and function. The sinus tract in the right pubic area had remained healed.

SUMMARY

The result of treatment with streptomycin in 2 patients with tuberculous tenosynovitis has been encouraging. It may be possible to avoid operative intervention completely in such patients by the use of this drug, with a considerable saving of time and money to the patient. Immobilization was not used in treating either of these patients. Streptomycin can be given in the clinic or the office under outpatient conditions, and, since the patient is seen twice a day, careful observation for toxic symptoms can be made. With the exception of heavy manual labor, it may be possible for most patients to continue their work.

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HYPERTENSIVE ENCEPHALOPATHY AFTER ADMINISTRATION OF BENZODIOXAN

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Benzodioxan has been recommended for the differential diagnosis of hypertension. When given to a patient in whom elevation of blood pressure is due to the release of epinephrine, the adrenolytic properties of the drug are reported to cause a definite and sustained fall in blood pressure.[1]

Administration of benzodioxan to the patient reported in this article was followed by a rise in blood pressure and precipitation of a typical attack of hypertensive encephalopathy. The circumstances suggested that the attack resulted from the sympathomimetic action of the drug in a susceptible person. Review of the available literature[1] and communication with

From the University of Washington Medical Department.
A supply of benzodioxan was made available by Merck & Co., Inc.

1. Goldenberg, M.; Snyder, C. H., and Aranow, H.: New Test for Hypertension Due to Circulating Epinephrine, J. A. M. A. 135:971 (Dec. 13) 1947; Cahill, G. F.: Pheochromocytomas, J. A. M. A. 138:180 (Sept. 18) 1948; Roth, G. M., and Kvale, W. F.: Pharmacologic Tests as an Aid in Diagnosis of Pheochromocytoma, Med. Concepts Cardiovas. Dis. 18:41 (May) 1949.

the manufacturer have not disclosed previous instances of such a reaction, although elevation of blood pressure, headache and dizziness have been observed.

REPORT OF CASE

The patient, O. S., was a short, plump and pleasant 55 year old housewife. She had had paroxysms of dizziness and blurred vision for three years. The husband said that he had noticed some right-sided twitching in his wife for years. The prior medical history was otherwise noncontributory.

The patient had been hospitalized with the same complaints two years earlier. At that time the blood pressure fluctuated between 140 and 204 mm. of mercury systolic and 80 to 110 mm. diastolic. A roentgenogram of her chest showed a heart of normal size with a prominent left ventricle. Traces of albumin were found in some specimens of urine. All other examinations showed normal conditions. Mild sedatives produced a temporary improvement, and the condition was diagnosed as essential hypertension.

After discharge the patient experienced a slow progression in the frequency and severity of her symptoms. She was not particularly alarmed until the attacks became associated with ulnar tingling of the right hand, which spread up the arm and affected her tongue and her speech. Later there were transitory jacksonian convulsions in these areas, followed by generalized headache. These episodes lasted for five or six hours. Afterward the patient would feel perfectly well. No vomiting or indigestion was ever noted.

During the attack which immediately preceded the current hospital admission the physician found a severe hypertension. The blood pressure subsided to a nearly normal level when the attack had passed.

On physical examination the ocular fundi showed a generalized grade 2 narrowing and sclerosis of the retinal vessels. Spasm was absent. The size of the heart appeared to be normal. A blowing systolic murmur was heard over the aortic area. It was accompanied by a tambour-like accentuated second aortic sound. The blood pressure on admission was 210 mm. of mercury systolic and 120 mm. diastolic with a pulse rate of 80 beats per minute. The reflexes were generally hyperactive. There were no evidences of residual neurologic disturbance. The pressure of the cerebrospinal fluid was normal.

The early morning blood pressure varied from 140 to 210 mm. of mercury systolic and 70 to 120 mm. diastolic. Repeated urinalyses showed occasional red and white blood cells and once a faint tract of albumin. Exhaustive hematologic and chemical studies showed normal conditions, as did a retrograde pyelogram and a stereoscopic roentgenogram of the skull.

A cold pressor test was made, with the following results: the preimmersion blood pressure stabilized at 158 mm. of mercury systolic and 91 mm. diastolic. Thirty seconds after immersion it rose to a maximum of 175 mm. of mercury systolic and 100 mm. diastolic. The pressure returned to preimmersion levels within six minutes.

When the response to the cold pressor test had subsided a histamine test was performed. The preinjection pressure averaged 170 mm. of mercury systolic and 90 mm. diastolic. Thirty seconds after injection it dropped to 118 mm. of mercury systolic and 80 mm. diastolic; subsequently it rose over a four minute period to a maximum of 190 mm. of mercury systolic and 100 mm. diastolic; then it fell slowly to normal. The test was accompanied by a pronounced flush and transitory headache.

When the blood pressure had stabilized, benzodioxan was given intravenously over a two minute period in a dose of 10 mg. per square meter. The preinjection blood pressure averaged 168 mm. of mercury systolic and 96 mm. diastolic. Thirty seconds after the start of injection it dropped briefly to 160 mm. of mercury systolic and 92 mm. diastolic, then rose steadily during the next six minutes to reach a value of 190 mm. of mercury systolic and 110 mm. diastolic. At this point the patient's speech became thick and garbled; her eyes appeared glazed. A moment later convulsive twitchings shook her right arm and distorted her neck and face. With the onset of the convulsions blood pressure readings were abandoned, and 500 mg. of amobarbital sodium (amytal sodium®) were given intravenously. The seizure lasted about three minutes. No residual neurologic involvement was noted. Five minutes later the patient had recovered her speech and was able to talk coherently, although sleepily. She asserted that the episode had mimicked her prior attacks perfectly. The similarity was confirmed by the intern, who had observed her spontaneous paroxysms.

The question arose whether this attack was coincidental or drug induced. That the sympathomimetic action of the benzodioxan was the causative factor was suggested by the following considerations: (1) close temporal relation between the injection of the drug and the reaction; (2) failure of other provocative tests to precipitate an attack, and (3) abortion of a subsequent spontaneous episode by administration of tetraethylammonium bromide.

SUMMARY AND CONCLUSION

Benzodioxan was administered to a woman who had had paroxysmal attacks of blurred vision, convulsions of the right side and hypertension. Injection of the drug was followed by a decided rise in blood pressure and a typical convulsive seizure. The attack subsided without residual signs after administration of amobarbital sodium.

This reaction was considered to result from the sympathomimetic action of benzodioxan in a susceptible person.

Council on Foods and Nutrition

This paper was prepared at the request of the Council and is one of a series appearing in THE JOURNAL. In the near future the entire series will appear in book form as the Council's Handbook of Nutrition. JAMES R. WILSON, M.D., *Secretary.*

NUTRITIONAL NEEDS IN ILLNESS AND DISEASE

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Physicians are puzzled by the inability of their colleagues who work in investigative nutrition to supply them with the simple accurate statements of the daily requirements of the essential nutrients of a healthy human being. To the uninitiated it would seem a straightforward request of easy solution. However, the elusive mechanisms by which many of the essential nutrients function, coupled with a paucity of biochemical technics by which specific deficiencies can be accurately detected, have limited these answers to approximations.

In laboratory animals, when dietary factors can be rigorously controlled and when the use of large numbers of subjects allow statistically sound conclusions, the requirements are reasonably well established for at least a few species. The nutritional requirements of the rat, for example, are known fairly well, but this achievement has required the concerted efforts of hundreds of workers over a period of decades.

When one considers the abnormal, that is, the diseased person, the problem of nutritional requirements becomes more complicated.

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There can be no question of the environmental importance of diet; in fact, one can justifiably say that food is the most important environmental factor affecting health. The food we eat not only is one of the most continuous elements of our environment but also assumes by far the most intimate relationship with us. The food we eat enters and does in fact constitute the very structure of our bodies. It has long been apparent that there exists a correlation between the nutritional environment and the form and capabilities of the individual and of his society. It is also an ancient observation that death and disease are guided to a large extent by diet. Within modern times irrefutable studies have shown in many parts of the world that diet conditions disease, diet influences growth and development and diet is a decisive factor in determining death rates.

Appreciation of the nutritional aspects of disease have been handicapped by two principal concepts: (1) The medical profession has been (and unfortunately in most quarters still is) trained to think of nutritional deficiencies in terms of overt and florid physical manifestations; for example, the flagrant signs of beriberi or scurvy. (2) The profitable returns from production and exploitation of nutritionally active substances have caused great pressure to be brought on both the patient and the physician, encouraging them to believe that many common physical disorders can be prevented and cured by profuse vitamin, mineral or protein medication. This philosophy exists at the expense of sound food habits in the home and sound nutritional diagnosis and therapy in the hospital and physician's office.

Although there are no established quantitative values for the requirements of the various nutritional substances in diseased states, it is possible to arrive at a reasonable dietary treatment of many diseases by an appraisal of experimental laboratory data and of clinical trial and error.

Such information as is available concerning the dietary needs of man in illness and disease is largely of two sources: (1) directed laboratory studies of diseased animals (including man) with a view to measuring in as objective a fashion as possible the nutritional status, and (2) clinical observations, either of the response to nutrient supplementations or observations of the effect of an illness superimposed on a prior clinical deficiency state. As a corollary to this method is the statistical procedure of comparing morbidity or mortality rates of populations with diverse dietaries.

Because the methodology essential to a nutritional point of view and adequate therapy is of relatively modern origin and distinctive character, we shall review the fundamentals.

NUTRITIONAL HISTORY

The nutritional status of a patient when first seen is in large part determined by the dietary intake for the preceding months. An initial step, then, in the evaluation of the reciprocal relationships of the present nutritional status and disease is an attempt to establish data regarding the diet history. It follows that the diet history is an integral part of the medical history. The inadequacy of ascertaining what the patient has eaten at the three immediately preceding meals is apparent. It is necessary to determine the food pattern for the preceding weeks and months. How often are certain foods—vegetables, citrus fruits, milk products and meat—consumed per day and per week and in what quantity? For the examiner, at least a basic knowledge of food composition, of average helping size and of local availability of various foods is of importance.

In the evaluation of the nutritional status of the patient by means of the history, the social history is of considerable value. Frequently there is good correlation between economic income and dietary adequacy. Familiarity with racial and religious food taboos, group diet customs and personal idiosyncrasies is valuable. Finally, it must be admitted that until the individual physician is convinced of the importance of nutritional environment in conditioning disease his histories will continue to be inadequate.

With a good diet history at hand, the physician with an elementary knowledge of normal nutritional requirements will be able to evaluate the patient's dietary. A convenient guide is the National Research Council's "Recommended Dietary Allowances." It is probably sufficient to be able to say that a particular patient has received adequate, marginal or inadequate quantities of various nutrients, such as protein, calcium, riboflavin or vitamin A. With this accomplished the physician is able to correlate the physical manifestations of disease present with the diet history and to design his therapy accordingly. Clinical specialists in nutrition are skeptical of the value in medical practice of elaborately computed estimates of the amount of each dietary essential consumed daily.

PHYSICAL EXAMINATION

Medical literature abounds with real or supposed physical manifestations of specific nutritional deficiency states. Abnormalities of skin, mucous membranes, hair, nails and neurologic signs are frequently attributed to various deficiencies. Although these signs may be sufficiently demarcated in the rare case to allow objective evaluation, characteristically the physical signs of deficiency states are nonspecific and multiple. The manifestations of the majority of deficiency states complicating disease are far more subtle than is commonly believed. It is not the purpose of this paper to discuss the physical signs (or symptoms) associated with poor nutrition.

LABORATORY EXAMINATION

A series of biochemical technics have been developed which are of some assistance in the evaluation of the nutritional state when a good laboratory is available. In the blood, total protein, albumin, globulin, hemoglobin, iron, ascorbic acid, vitamin A and carotene, as well as some other nutrients, can be measured. Blood volume can also be determined. This is highly desirable in interpreting most blood chemical data, for generally it is the total circulating quantity of nutrient that is important, not simply the percentage. Urinary excretion tests of various types are available. The serum calcium and phosphorus and phosphatase values are almost specific in rickets. However, in most instances a definite diagnosis will not be obtained from chemical data alone.

Roentgen examination can be of assistance in the diagnosis of rickets, scurvy, osteomalacia and osteoporosis. The skeletal changes in rickets and scurvy are quite specific. Recently roentgenologists have described a so-called deficiency pattern in intestinal

studies after barium test meals. Here again the abnormalities are not specific for nutritional disease but do suggest, none the less, careful consideration of the diet history and the diet in prospective therapy.

NITROGEN METABOLISM METHODS

The significance of protein in nutrition warrants a discussion of the fundamental methods in the study of nitrogen metabolism. Protein has come to assume a new role in nutrition with the development of knowledge of the more fundamental aspects of the biochemistry of the constituent amino acids. In addition to its conventional function as a source of anabolic nitrogen, a source of calories and a delicacy for the palate, protein has taken the position of a therapeutic agent, comparable to digitalis or the sulfonamide compounds. This development, largely of the last two decades, has resulted from the observations that certain of the amino acid constituents of dietary protein are "essential" and have unique roles in metabolism. These essential amino acids have much the same position in human food requirements and in diet planning as the vitamins and minerals. Much emphasis in investigative work is now placed on these essential nutrients rather than on the food proteins representing the natural mixtures of these substances.

With these developments an interesting concept has arisen, which is in fact still another application of a generality stated over a hundred years ago by the chemist Justus von Liebig, a pioneer in problems of nutrition. The generality is known as the "Law of the Minimum" and states that growth and development (Liebig referred to plant requirements) are determined by the availability of that essential substance present in the least amount. The problems of protein and amino acid requirements are concerned with the requirements of each of the essential materials present in the diet, with their concentrations in the diet and with the effect that diseased states may have on these requirements. In practical terms it is of interest to know whether additions to the diet, either of protein or of the specific amino acids, will favorably influence the course of disease.

The most commonly used procedure in the study of nitrogen metabolism, both in laboratory animals and human beings, has been the measurement of nitrogen balance. If one measures the dietary nitrogen intake and the total nitrogen excreted (or lost) in the urine and stools, a balance sheet may be made which by difference will represent the gain or loss of nitrogen by the organism—the values being positive or negative balance respectively. An organism is said to be in nitrogen balance when the intake is equal to the output. Since the amount of nitrogen in the diet may not be absorbed in entirety, depending on the nature of the protein and the efficiency of the intestinal tract, appropriate corrections must be made in order to calculate the absorbed nitrogen. In the normal person the fecal nitrogen is a relatively constant value but will vary with the digestibility of the dietary protein. The amino acids obtained from the diet either as such or as hydrolytic products are the principal source of body proteins. Comparisons of the performance of animals and human beings when receiving various proteins have emphasized the importance of that fraction of the dietary nitrogen which is retained in the body. The percentage of absorbed nitrogen that is retained by the body is designated "the biologic value" of the protein, and it has proved practicable to judge various dietary proteins by this means. Allison and Anderson [1] have expressed these relationships as follows:

$$B\,V. = \frac{AN-(UN-EN)}{AN} \times 100$$

where UN represents urinary nitrogen; BV, biologic value; AN, absorbed nitrogen, and EN is the endogenous nitrogen. Endogenous nitrogen represents the nitrogen which is excreted continuously as what might be called "breakage" nitrogen—the result of essential biochemical procedures which draw on body nitrogen and result in an irretrievable net loss. Thus on a nitrogen free diet a subject will continue to excrete diminishing amounts of nitrogen.

Another useful method for the study of nitrogen metabolism has been the measurement of the relationship of depletion or supplementation to measurable variables, for example, body weight in the growing animal or, somewhat more specifically, the measurement of the rate of depletion or regeneration of serum proteins under varying conditions of protein intake. Whipple and co-workers [2] at the University of Rochester have contributed much of the latter evidence. These technics offer not only means of comparing the effect of variation of the quality and quantity of nitrogen intake in similar animals but also opportunity to study the response of variable animals under conditions of similar nitrogen intake. The majority of the available evidence in human beings is of the nitrogen balance type.

RESPONSE TO THERAPY

Much of the available clinical evidence in the diagnosis of nutritional disease is obtained from supplementation of the diet and study of the patient's response.

Dietary manipulations in healthy persons or in persons with chronic nutritional deficiencies are a comparatively simple procedure. However, diet therapy in acutely ill patients is considerably more difficult, because of anorexia.

A systematic method of procedure in nutritional therapy of diseased patients will simplify considerably the physician's task. One may consider that there are three basic levels of intensity of nutritional therapeusis: (1) adequate diet, (2) supplementary levels of nutrients and (3) therapeutic levels of nutrients. Of these an adequate diet is the most fundamental. It represents a quantity and selection of food that is available to almost all persons in this country, but it can be accomplished in many instances only by direction of food selection and planning of food budgets and supplies. In a sick person the aim in therapy must be to encourage a return to maintenance of adequate diet. The dietary recommendations of the Food and Nutrition Board of the National Research Council are the most useful standards for this basic diet. All physicians should be familiar with these recommendations and know how to obtain them from foods.

When the history indicates that an adequate diet cannot be achieved, supplementary additions of the essential nutrients are desirable. In many instances

1. Allison, J. B., and Anderson, J. A.: The Relation Between Absorbed Nitrogen, Nitrogen Balance, and Biological Value of Proteins in Adult Dogs, J. Nutrition **29**: 413, 1945.

2. Robscheit-Robbins, F. S.; Miller, L. L., and Whipple, G. H.: Hemoglobin and Plasma Protein Production—Various Proteins, Concentrates, and Digests Influence Blood Protein Production in Anemia and Hypoproteinemia, J. Exper. Med. **83**: 463, 1946.

addition by prescription of special foods of high nutritional potency may suffice. Thus, addition of citrus fruits, yeast, or liver may accomplish the purpose with the greatest economy. If this is impracticable, the addition of low cost, low potency multivitamin preparations may accomplish the same purpose. When synthetic vitamin preparations are used for supplementary purposes, they should be added in amounts to approximate the National Research Council's daily recommendations. Every attempt should be made to enable the patient to maintain a diet which will accomplish nutritional balance without supplementation. Such a diet, skilfully proposed and encouraged, will serve both as a specific therapy in the presence of nutritional disease and as an important application of preventive medicine.

Therapeutic levels of vitamin supplementation are indicated in the presence of evidence of one or more specific deficiency diseases. Since it is well established that deficiency of a single essential nutrient rarely occurs in human medicine, therapy should include supplementation with 5 to 10 times the National Research Council recommendations of the specific nutrient involved with 1 to 5 increments of the remaining. Thus, a person with pellagra would be treated with 100 to 200 mg. of nicotinic acid per day with supplementary levels of the remaining vitamin B complex factors. This systematized procedure and the composition of the medications has been discussed by Jolliffe.[3]

NUTRITIONAL REQUIREMENTS IN DISEASES OF THE GASTROINTESTINAL TRACT

The physician is called on to apply diet therapy most frequently in the management of disorders of the gastrointestinal tract and particularly in disorders of the stomach. Peptic ulcer is so prevalent as to be an everyday problem of most practitioners.

The treatment of peptic ulcer is designed, first, to relieve the patient of his symptoms and, second, to attain permanent healing of the ulcer. Those patients who do not have a significant degree of obstruction—probably 75 per cent of all patients with ulcer—almost always are well nourished. Their appetite, digestion and assimilation have not been impaired by the disease. There is little evidence to indicate that these patients have been predisposed to their disease by dietary inadequacy or that the course of the disease will be altered by improving the nutritional quality of their diet. The eventual success or failure of symptomatic dietary treatment, however, will to a large extent be based on the degree of cooperation of the patient. In this situation the physician must help a patient learn and practice new food habits and hence meet on common ground with the public health nutritionist who attempts to teach entire populations new food habits.

The therapy of peptic ulcer is aimed first at relieving symptoms. Bland foods, such as milk and eggs, which are commonly used, are, fortunately, at the same time nutritious. The widespread belief that patients with peptic ulcer should be fed a bland, soft diet may lead to avoidance of many foods rich in other nutrients, such as vitamins of the B complex, vitamin A, carotene and various minerals.

The 25 per cent of ulcer patients with obstructive lesions pose a more difficult nutritional problem. The dietary deficit in this instance is one of calories and protein. Aside from the maintenance of water and electrolyte balance in the presence of vomiting and lavage, the principal difficulty is one of supplying sufficient calories and protein for maintenance of energy and nitrogen balance until medical treatment leads to subsidence of the obstruction or the obstruction is relieved by surgical methods. It is well to remember that in this, as in all instances of caloric deficit, the prior demand for calories will make other protein and structural requirements of the body subservient. Thus, in the absence of sufficient calories, an otherwise normal supply of protein will be inadequate, because of its redirection into energy channels.

The frequent use of small, nutritious, liquid feedings will suffice in mild cases of obstruction. Patients requiring parenteral supplementation of caloric intake will likewise require parenteral administration of vitamins. However, the urgency of caloric requirement will generally force the decision to surgical intervention before a vitamin deficiency becomes of serious consequence.

In the present state of knowledge, the parenteral use of amino acid compounds seems justified as a preparation for surgical intervention and in patients who respond so slowly to medical treatment that the period of low protein intake and consequent negative nitrogen balance extends over many weeks.

The proposal that frequent oral feedings with protein hydrolysate and a comfiercial carbohydrate preparation [4] is an advance in diet therapy of peptic ulcer has not been confirmed. It seems unlikely that this form of diet has advantages over more economical and equally nutritious foods in general use. There is evidence that, contrary to theoretical expectations, the buffering action of the amino acids and polypeptides may be offset by an apparent stimulation of the acid-secreting cells of the gastric mucosa.[5]

The internist is often responsible for the care of patients after surgical treatment for ulcer. Several careful reports [6] have indicated that, although patients who have undergone gastrectomy are generally able to maintain their weight—and few of them develop the pernicious anemia anticipated—many of them (up to 25 per cent) according to Zollinger and Hoerr [7] exhibit postprandial symptoms of serious consequence. The symptoms have been given the expressive but ungracious name of "the dumping syndrome." In many patients two distinct phases of the syndrome follow meals. The first is believed due to rapid and extensive filling of the jejunum and the second is believed to be consequent to a hypoglycemic period following the initial rapid absorption of carbohydrates. These symptoms may be controlled effectively by assuring that the patient procure not less than 50 per cent and preferably more of his total caloric requirement from protein and fat, thus reducing the intake of rapidly absorbable carbohydrate, which seems to be one immediate cause of the symptoms.

3. Jolliffe, N.: The Preventive and Therapeutic Use of Vitamins, J. A. M. A. 128:613 (Oct. 27) 1945.

4. Co Tui; Wright, A. M.; Mulholland, J. H.; Garvin, T.; Barcham, J., and Gerst, G. R.: Hyperalimentation Treatment of Peptic Ulcer with Amino Acids (Protein Hydrolysates) and Dextri-Maltose, Gastroenterology 5:5, 1945.

5. Hodges, H. H.: Protein Hydrolysate Therapy for Peptic Ulcer, Gastroenterology 8:476-493, 1947.

6. Custer, M. D., Jr.; Butt, M. R., and Waugh, J. M.: The So-Called "Dumping Syndrome" After Subtotal Gastrectomy, Ann. Surg. 123:410, 1946.

7. Zollinger, R. M., and Hoerr, S.: Gastric Operations: Troublesome Postoperative Symptoms with Special Reference to Carbohydrate Ingestion, J. A. M. A. 134:573 (June 14) 1947.

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That only a small number of patients with total gastrectomies have required treatment for pernicious anemia has been surprising. Patients subjected to this procedure should be carefully observed, however, since this complication may produce irreparable damage to the nervous system before treatment is begun.

In attempts to relieve the pain of peptic ulcer almost every patient is given an antacid medication of some sort. That this procedure may do more than reduce gastric acidity and alleviate symptoms for a few hours is indicated by the finding of Robinson and his co-workers [8] that certain antacids as magnesium trisilicate act as efficient adsorbers of thiamine, thus making dietary thiamine partially unavailable. Although it is well known that several of the B complex vitamins are unstable in vitro when exposed to alkaline solutions, there is little evidence that the brief encounter of the vitamins with antacids in the stomach will lead to a serious impairment of available vitamins.

Probably the most frequent contributing cause in nutritional deficiency is diarrhea. Irrespective of the nature of the diet, if the passage of food through the gastrointestinal tract is so rapid that absorption is limited, poor nutrition will result. In addition, diarrhea often characterizes diseases in which the absorptive capacity of the mucosal surfaces has been impaired. When infections occur along the tract, hypermotility appears, anatomic changes slow the absorptive process and the systemic reactions to the infection may increase requirements. These factors, working concertedly, lead to malnutrition and, in a vicious cycle, to acute deficiency states. There is, in addition, the uncertain effect these circumstances may have on the intestinal flora and its natural supply of essential nutrients. Aside from the use of diet as symptomatic treatment, the greatest importance to the outcome of the disease will attend the degree to which requirements for essential nutrients, including proteins, and calories are met. Severe diarrhea more than any other medical problem demands complete parenteral nutrition. This is at present impossible, because of lack of means of supplying sufficient calories.

Considerable information has been obtained concerning the means of meeting water and electrolyte requirements.[9] The most crucial problem in the treatment of acute diarrhea is that of supplying the energy deficit. Glucose solutions are limited by their low calory concentration when considered in terms of hypertonicity and fluid volume. Protein digests will supply nitrogen requirements, but, unless energy requirements have been supplied, they will be unceremoniously burned for calories and the need for anabolic nitrogen will persist.

Chung and Viscorova [10] have recently advocated a program of forced feeding (orally) in diarrhea of infants, rather than fasting as has been the custom. This procedure has the advantage that such restricted absorption as remains will be used to the fullest extent. Clinical evaluation of this procedure suggests favorable results.

Parenteral supplementation with the water-soluble vitamins is indicated with persistent diarrhea. Preparations of vitamins A and D for parenteral use are now becoming available and should be used. The water and electrolyte balance may be maintained with parenterally administered mixtures. Darrow [11] has recently pointed out the need for potassium replacement in diarrhea of infants. Whether this occurs also in adults with severe diarrhea is not established. Until a suitable concentrated source of calories for parenteral use, such as an emulsion of fat, is developed, the attempt to supply calories must be for the most part by the oral route. There is little if any evidence to support the contention that hydrolyzed proteins in the form of amino acid polypeptide mixtures have any advantage over natural protein as a source of dietary nitrogen or calories in diarrhea. In addition, they are not palatable and are considerably more expensive.

The notable exception to this criticism of protein hydrolysates is in the dietary treatment of absorptive disorders due to a specific deficiency of proteolytic enzymes, as in pancreatic disease.[12] In this instance the oral use of amino acids is probably more satisfactory than an attempt to supplement the deficient proteolytic enzymes by orally administered, enteric-coated enzyme preparations.

It has been pointed out by several authors that the use of certain highly active adsorbing agents, as kaolin or fuller's earth, in the symptomatic treatment of diarrhea may not be desirable, since these compounds have been shown to adsorb and thus make unavailable dietary thiamine and perhaps other essential dietary constitutents.[13] These adsorbing agents have long been used by biochemists to concentrate natural sources of B complex vitamins. Until thiamine was synthesized, a fuller's earth adsorbate of a rice polish extract was for a time the international standard of thiamine. This standard was abandoned when it was shown that the rat could utilize only 50 per cent of the adsorbed vitamin.

The initial discovery that in monkeys maintained on a diet deficient in a factor called "vitamin M," later shown to be folic or pteroylglutamic acid, diarrhea developed in addition to pancytopenia has now assumed clinical importance. The similarity of the "sprue syndrome" in man led Darby and Jones [14] to test pteroylglutamic acid as a therapeutic agent in human beings. Previous experience in many clinics had confirmed the suggestion that the anemia of sprue was often responsive to liver extracts given parenterally. Darby found that 15 mg. of synthetic pteroylglutamic acid given intramuscularly daily relieved the symptoms within two weeks and improved the hematologic deficiency. Spies [15] has confirmed these observations.

It may be inferred, then, that sprue is a specific deficiency disease since it appears to be cured by pteroylglutamic acid. The etiology is confused, however, and the relationship of these observations to the epidemiology of sprue is not clear. If the absorptive defect can be corrected by abolishing the diarrhea, the serious disorders of calcium metabolism, hypoprothrombinemia,

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15. Spies, T. D.: Effect of Folic Acid on Persons with Macrocytic Anemia in Relapse, J. A. M. A. **130**: 474 (Feb. 23) 1946.

hypotocopherolemia and multiple water-soluble vitamin deficiencies are no longer a problem.

The past ten years have produced remarkable advances in our knowledge of the treatment for pernicious anemia. The development of pteroylglutamic acid (folic acid) led to a water-soluble vitamin which at least partially treats the hematologic defect in pernicious anemia. It has been repeatedly shown, however, that folic acid therapy will not prevent progression of the neurologic components of pernicious anemia.[16] Within the past year a new member of the water-soluble vitamin complex, vitamin B_{12}, has been announced.[17] Preliminary trials indicate that this vitamin given parenterally will produce effective remissions of all the manifestations of pernicious anemia.[18] Other clinical trials of this material have indicated[19] that vitamin B_{12} appears to be identical with the antipernicious anemia principle of liver. One unit of liver activity is approximately equivalent to 1 microgram of vitamin B_{12}. Observations by Berk and his co-workers[19] show that vitamin B_{12} administered orally to patients with pernicious anemia has little if any hematopoietic activity. Simultaneous administration of normal gastric juice with orally administered vitamin B_{12} produced a hematopoietic response. This evidence suggests the presence of an "intrinsic" factor necessary for the utilization of dietary sources of the "extrinsic" factor, which is presumably vitamin B_{12}.

The nutritional failure of patients with ulcerative colitis is characteristic of this disease. Welsh and his co-workers[20] have shown in studies on a few patients that the most pressing nutritional need was for protein. They found that the fecal nitrogen loss became the major pathway of nitrogen excretion and that this loss of nitrogen was proportional to other signs of activity of the disease. They believe that exudation and tissue destruction with continuing hemorrhage are the principal causes of the negative nitrogen balance—and not the hypermotility in the small intestine with poor absorption as is generally supposed. Other investigators[21] have shown that patients with colitis show abnormally low serum levels for almost every vitamin that can be measured. Caloric deficiency is undoubtedly of equal importance to protein deficiency in ulcerative colitis.

The diet therapy must be inclusive. Ideally the maximum degree of nutrition, both quantitatively and qualitatively, is sought with the least possible amount of mechanical irritation of the colon. Since most of these patients have anorexia and are well aware that eating often precipitates a new bout of diarrhea, the task is not simple. In so far as the oral nutrition falls short of conservative estimates of daily requirements of vitamins, proteins and calories, parenteral supplementation should be used. Here again, the attainment of caloric balance is almost impossible with present procedures, and this failure will often confound the best attempts to correct a mounting nitrogen deficit.

A discussion of nutrition and diseases of the intestinal tract should include at least a comment on the use of liquid petrolatum, a commonly used gastrointestinal medicament. Experimental nutritionists have known for many years that inclusion of hydrocarbon oils, "mineral oil," in animal diets may lead to fat-soluble vitamin deficiencies.[22] Javert and Macri[23] pointed out the potentially serious consequences of the use of liquid petrolatum for laxation during pregnancy through the consequent lowering of the prothrombin level, presumably a manifestation of vitamin K deficiency. This effect is produced by the preferential solubility of the fat-soluble vitamins in the largely unabsorbable oil. There is, in addition, evidence[24] that, if liquid petrolatum is sufficiently subdivided in the intestinal emulsion, it may be absorbed. The absorption of liquid petrolatum leads in experimental animals and human beings to demonstrable depositions of the material in the mesenteric lymph nodes and the liver. Typical foreign body reactions occur about these sites.[25] A recent report by Mahle and Patton[26] summarizes the available evidence pertinent to this problem. The use of hydrocarbon oils for laxation does not seem to be a sound procedure.

NUTRITION IN HEPATIC DISEASE

The magnitude of the enthusiasm in clinical circles supporting dietary treatment of acute and chronic disease of the liver justifies some reexamination of the pertinent evidence.

The etiology of cirrhosis of the liver, a common medical problem, remains obscure. The hypothesis that this chronic disease of the liver in man is caused by a nutritional deficiency has not been proved; however, a disease has been produced in several species of animals by dietary restrictions which simulates human cirrhosis in most respects. There are many reports in the medical literature concerning the effectiveness of a variety of diet therapies and the use of one or several nutritionally essential factors, as separate supplements in the treatment of hepatic disease in human beings. The conclusions of these investigations are in disagreement. Whatever the outcome of these researches, the clinician will do well to remain a pragmatist. Common experience indicates that cirrhotic patients often get along well when treated with nutritionally adequate diets alone.

The concept that ethyl alcohol alone acts as a "toxin" to damage liver cells and that its use leads to cirrhosis has not been confirmed. In experimental animals alcohol seems to act synergistically with other mechanisms to produce cirrhosis, but alone does not. The dietary inadequacy which follows in the wake of alcoholism taken with the high incidence of cirrhosis in populations that subsist on marginal diets suggests that this is, in part, a deficiency disease.

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17. Rickes, E. L.; Brink, N. G.; Koniuszy, F. R.; Wood, T. R., and Folkers, K.: Crystalline Vitamin B_{12}, Science **107**: 396, 1948.

18. West, R.: Activity of Vitamin B_{12} in Addisonian Pernicious Anemia, Science **107**: 398, 1948.

19. Berk, L.; Castle, W. B.; Welch, A. D.; Heinle, R. W.; Anker, R., and Epstein, M.: Observations on the Etiological Relationship of Achylia Gastrica to Pernicious Anemia: X. Activity of Vitamin B_{12} as Food (Extrinsic) Factor, New England J. Med. **239**: 911, 1948.

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23. Javert, C. T., and Macri, C.: Prothrombin Concentrations and Mineral Oil, Am. J. Obst. & Gynec. **42**: 409, 1941.

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25. Stryker, W. A.: Absorption of Liquid Petrolatum (Mineral Oil) from Intestine: Histologic and Chemical Study, Arch. Path. **31**: 670 (June) 1941.

26. Mahle, A. E., and Patton, H. M.: Carotene and Vitamin A Metabolism in Man: Their Excretion and Plasma Level as Influenced by Orally Administered Mineral Oil and a Hydrophilic Mucilloid, Gastroenterology **9**: 44, 1947.

The belief that a high carbohydrate diet protects the liver from subsequent injury stems from the work of Rosenfeld [27] and Opie and Alford.[28] More recent work has indicated that the protein in the diet and available to the liver at the time of damage is of considerably more importance. The significance of the protein stores in preventing liver damage is continually emphasized in animal work and has received some clinical affirmation.

An additional complexity has been the evaluation of the place of lipotropic agents in the treatment of hepatic disease. Of these, choline, methionine and inositol have received attention. A dietary deficiency of choline will lead to a fatty liver in the rat and dog. Several clinical reports have indicated favorable results from the treatment of Laennec's cirrhosis with 1.0 to 5.0 Gm. of choline chloride daily.[29]

High carbohydrate diets or the parenteral use of carbohydrate in the treatment of a damaged liver or in anticipation of liver damage, as before anesthesia, is based on the belief that as liver glycogen is laid down liver cell lipids will be removed. Ravdin and his co-workers [30] pointed out that adequate protein sources and sufficient carbohydrate to spare this protein from energy consumption is the important aspect of this apparent lipotropism of carbohydrate.

The importance of protein in protection of the liver against injury has been confirmed by many workers.[31] Methionine, an essential amino acid, and proteins rich in this amino acid act as does choline in mobilizing liver lipids. Both choline and methionine, the common attribute of which is believed to be the presence of a labile methyl group, act to protect the liver in dogs maintained on low protein diets when chloroform is given as a poison. Although inositol, an isomer of glucose, has been shown to exhibit lipotropic properties under certain conditions in laboratory animals, there is no evidence to support the use of inositol in the treatment of hepatic disease in human beings. The crucial question which remains, however, is whether these substances, which are effective when given experimentally preparatory to liver damage, are also of value clinically when administered following the liver damage. Many clinicians assume that this is true and advocate not only high protein (100 to 150 Gm. per day) diets but supplementation with choline and/or methionine given orally. We believe that this remains an open question.

Since the liver is known to be intimately concerned with the metabolism and storage of many of the vitamins, it would be expected that in a chronic progressive disease such as cirrhosis, in which the effective functional liver tissue is steadily diminished, multiple vitamin deficiencies would result. Deficiencies of both vitamins A and D have been found, frequently requiring supplementary therapy. Vitamin K therapy parenterally will support the prothrombin level until liver failure becomes marked. Therapy with supplementary levels and preferably with natural sources, as dried yeast, provided this is given in adequate amounts (40 to 50 Gm. daily), supplies B complex vitamins and, in addition, contributes protein.[32]

Similar considerations apply to hepatitis of virus origin. The characteristic anorexia and nausea of the early clinical stages of the disease present serious problems. Parenteral nutrition with protein hydrolysates and dextrose is often necessary. The vitamin requirements in infectious hepatitis are not known to be altered. Supplementary dosages of vitamins are probably desirable as a precautionary measure. The tendency to chronicity with occasional relapse of infectious hepatitis demands thorough diet education of the patient with continuation of optimal protein and vitamin intake for many months.

The concept of the value of a low fat diet in the therapy of hepatic disease, which rested practically on the observed intolerance of fat of some patients with hepatic disease and theoretically on the poorly founded belief that fat in itself when present in the liver was deleterious, has been challenged by several reports. Hoagland and others [33] found that convalescence from hepatitis was in fact shortened by liberal fat intake in the diet, presumably by reason of the improved palatability and thus better consumption of the high protein, high vitamin diet used.

NUTRITIONAL NEEDS IN RENAL DISEASE

With the exception of the treatment for infection and some neoplastic and traumatic disorders, the therapy of renal disease is nonspecific and largely symptomatic. The concepts behind most of the commonly used diet therapy methods are of ancient origin. Fishberg [34] states, "The regulation of the diet forms the corner stone of the treatment of glomerulonephritis."

One of the fundamental tenets has been that, since protein metabolism calls on renal excretion of end products and since fat and carbohydrate are burned to water and carbon dioxide which may be disposed of extrarenally, protein should be limited in the diet of patients with impaired renal function in order to afford physiologic "rest." Since the elevation of serum nonprotein nitrogen is an easily measured index of renal functional impairment it has been considered prime evidence of the relationship in nitrogenous intake, impaired excretory function and uremia. It is in fact frequently observed that the amount of nitrogen in the diet will influence the level of the serum nonprotein nitrogen and recently Addis and his co-workers [35] have shown that in healthy adults the level of blood urea nitrogen is influenced by the amount of nitrogen in the diet.

Admittedly, nitrogen excretion is only one of many functions of the kidney. It may be questioned, then, whether the amount of physiologic "rest" and "symptomatic" treatment of the nitrogen retention which

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35. Addis, T.; Barrett, E.; Poo, L. J., and Yuen, D. W.: Relation Between Serum Urea Concentration and Protein Consumption of Normal Individuals, J. Clin. Investigation **26**: 869, 1947.

one obtains by diet restriction of protein is significant or beneficial. There is no evidence that a liberal allowance of protein, i. e., 60 to 80 Gm. per day, is harmful even in the presence of azotemia. There are many who question the restriction of diet protein in the presence of renal disease. The part that this restriction, coupled with loss of protein through the urine, plays in the development of asthenia, anemia, hypoproteinemia and edema may be greater than is realized.[36] Also pertinent to the dietary treatment of diseases of the kidney is the evidence that high protein diets lead to higher urea clearance values in normal experimental dogs as compared with dogs on low protein diets, and similarly the renal blood flow is increased by a high protein diet.[37]

There are other experimental observations which may be of importance in this problem. The discovery by Masugi [38] that a form of glomerulonephritis simulating the human variety could be produced in rats by the injection of "anti-rat kidney" rabbit serum, led Farr and Smadel [39] to investigate the effect of diet on the course of this experimental nephritis. It was found that high protein diets led to a higher mortality among the diseased rats.

The ancient belief, common still among the laity, that red meats are more harmful than white meats to patients with renal disease has no basis in fact. Neither is there reason to believe that plant proteins are more beneficial than animal proteins, or vice versa. The same principles of nutritive value based on the biologic value are applicable to the diets of these patients. Aside from a variable content of fixed base, as sodium, which may be of importance to patients with water retention or edema, there are no known protein constituents harmful to patients with nephritis.

The observation that animals will develop vascular and renal lesions after large amounts of dietary protein has been confirmed by several laboratories.[40] Knowledge of these phenomena in human beings is lacking.

The problem for the clinician, then, is one of diet regulation which will least retard and most stimulate the remarkable ability of the kidneys to restore damaged function. Except in acute renal emergencies characterized by lack of urine excretion, usually of short duration, the protein intake should be sufficient to maintain nitrogen balance. In a patient at rest without fever, this may be as little as 30 to 40 Gm. per day. However, since appetite is often poor and the caloric requirement satisfied with difficulty, there would seem to be few occasions when less than 1 Gm. of protein per day per kilogram of body weight should be given. In the presence of significant proteinuria the dietary protein intake should be supplemented with an amount of protein equivalent in grams to that lost in the urine. Restriction of salt and selection of protein sources of low salt content are indicated in the presence of edema or salt retention. When the appetite and salt tolerance will allow, the use of dietary protein as a source of urea and anions as stimulants to diuresis may sometimes be useful. However, administration of urea and ammonium chloride is generally more effective.

The dietary management of edema occurring with nephritis has recently been discussed by Thorn and Tyler.[41] The limitation of the sodium intake is of prime importance. The inability of the diseased kidney to excrete the sodium ion is the basis of most "renal" edema. Since much of the sodium (as sodium chloride) in food is added during the preparation or at the table, restriction of these practices will decrease the salt intake to less than 5 Gm. per day. A daily salt intake of less than 1 Gm. per day (often required) will necessitate elimination of all added salt and avoidance of salted foods, including bread, butter and bakery products. Such a diet will often require vitamin supplementation, since the natural vitamin content of the diet may be low, especially in riboflavin.

Acid ash diets may be of assistance in augmenting diuresis. The net ash of the diet is effective in diuresis because residual metabolic anions must be excreted in combination with fixed base. Thus, an acid ash diet acts to encourage the kidney to eliminate sodium and allow water to be lost. If the sodium intake is adequately controlled, there is no real reason to restrict the water intake, since the water retained will be determined by the salt retained. The usefulness of water itself as a diuretic agent has been reemphasized by Schemm,[42] who advocates a low sodium, high fluid intake for patients with edema.

Because of their unpalatability, high salt content and lack of evidence that hydrolyzed proteins possess any advantages over native proteins, oral therapy with these materials is of questionable value. In addition, they are considerably more expensive. Parenteral amino acid therapy is occasionally used as an emergency means of supplementing a deficient oral intake of protein, but, unless caloric intake is adequate, much of the parenterally administered protein will simply serve as an expensive source of calories. The use of whole blood or plasma or derived plasma proteins to raise levels of serum protein remains an experimental and as yet impractical solution to the problem of hypoproteinemia of renal disease. Although the mechanism is unknown, there would seem to be an unrecognized metabolic defect in the patient with nephritis which prevents active or efficient reconstruction of plasma proteins. Until this problem is better understood, dietary therapy of the hypoproteinemia of nephritic patients is distressingly ineffective.

There is no evidence of specifically increased requirements of the vitamins or minerals in renal disease except possibly in "salt-losing" nephritic patients and in the potassium deficiency occurring after massive diuresis. The human counterpart of acute hemorrhagic nephritis [43] seen in young rats maintained on choline deficient diets has not been observed.

NUTRITIONAL NEEDS IN UROLITHIASIS

Diet therapy is an important adjunct to the surgical treatment of urolithiasis. There is good experimental evidence that inadequate diets may lead to calculi forma-

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tion in the urinary tract of animals [44] and suggestive epidemiologic evidence that the prevalence of urolithiasis in the Orient, for example, is directly related to the diet of the population affected. The value of dietary regulation lies in the prevention and the arrest of growth of stones. Diet therapy will rarely dissolve formed stones. Laboratory evidence indicates that strongly acid urine in the presence of high urinary purine excretion favors formation of uric acid and urate stones. Reduction of purine-rich foods and maintenance of neutral or alkaline urine by dietary methods is indicated when the stones are of purine origin.

Calcium-containing stones are primarily influenced by the amount of calcium excreted through the urine and the p_H of the urine. Hypercalciuria may be the result of dietary manipulation but is not usually caused by this. More significant causes of hypercalciuria are metabolic disorders such as hyperparathyroidism or the calcium mobilization consequent to bedrest. The chemical composition of the calcium-containing stones is largely determined by the reaction of the urine. Diet management should include insurance of adequate and balanced amounts of calcium and phosphorus. Oxalate intake should be reduced since calcium oxalate stones are common. When the hypercalciuria is of metabolic origin, maintenance of large volumes of neutral urine is of prophylactic value until the defect in calcium metabolism can be corrected. Calcium phosphate stones, occurring in alkaline urine, are a particular complication of hyperparathyroidism. The importance of maintaining an acid reaction in the urine is great. The same precaution pertains to the care of patients with prolonged immobilization when the atrophy of disuse allows large amounts of skeletal calcium to be excreted in the urine. The prolonged adherence to an alkalinizing regimen, as in the treatment of peptic ulcer, predisposes to calcium phosphate stones.[45]

The importance of vitamin A deficiency in initiating epithelial defects which lead to stone formation is still debated. An adequate allowance of vitamin A or carotene in the daily diet should be insured. The importance of nutrition in the etiology of urolithiasis is well summarized by Lowsley and Kirwin [46] as follows:

> That lithiasis is a deficiency disease is borne out by the notably decreased incidence of urinary stone—particularly bladder stone—in civilized countries in childhood since the institution of modern diets which prevent avitaminosis. . . . Fresh vegetables, milk and cod-liver oil have probably contributed more than any other factors to this lessening of the incidence of urinary stone in childhood.

NUTRITIONAL NEEDS IN CARDIOVASCULAR DISEASE

Diseases of the vascular system with their ramifications constitute a common medical problem for the physician and, because of their frequency and devastating course, now represent the greatest single menace to the health of the general population. Both the knowledge of etiology and treatment of these diseases remain unsatisfactory.

The widespread occurrence and slowly progressive course of vascular sclerosis, the most fundamental of cardiovascular diseases, suggest the presence of a similarly widespread and continuing environmental factor which may be in part responsible for this disease. Diet is undoubtedly the single most important environmental factor in present day civilization in this country and deserves thorough study in relation to this disease.

Experimental work has been done in animals which seems to incriminate the cholesterol moiety of the diet as a responsible factor in vascular sclerosis.[47] The earlier work with cholesterol was done with rabbits and chickens and may be criticized in that the atherosclerosis produced was in herbivorous species which normally do not ingest cholesterol and have inefficient biochemical mechanisms for its disposal. More recently similar observations have been made in dogs which were also fed thiouracil.[48]

Selye and Stone [49] have described vascular lesions produced in several species by the concomitant conditions of a high protein, high sodium chloride diet and injections of large amounts of desoxycorticosterone acetate. Selye calls the associated physiologic adaptive reactions the "alarm reaction." Investigation of this response may illuminate the entire problem of vascular sclerosis.

The restriction of protein intake in patients with hypertension is an ancient practice. Even in the presence of demonstrable renal damage stringent protein restriction with the intent of lowering the serum nonprotein nitrogen is not justifiable. There would seem to be no complication of cardiovascular disease aside from the brief cardiac emergency states requiring less than the normal allotment of 60 to 70 Gm. of protein per day. Neither is there evidence to indicate that excessive amounts of protein are of value. The belief that the high specific dynamic action of protein leads to excessive demands on the heart is of no practical importance. Of greater significance may be the observations that administration of ammonium salts, commonly used as diuretics in cardiac disease, causes a large increase in heat production and consequently in cardiac work.[50]

The management of cardiac edema by restriction of salt as outlined by Allen and Sherrill [51] is theoretically and in practice similar to the management of the edema of nephritis previously discussed.

The use of restricted salt diets is often advisable in cardiac disease as a prophylactic measure. Despite the small hardship it may work on the patient, the physician is often able to anticipate the development of congestive failure or peripheral edema and delay these misfortunes by means of low salt diets. Again, in anticipation of congestive failure when visceral edema impairs utilization, supplementary levels of vitamins are indicated.

Management of the caloric balance in cardiovascular disease is of extreme importance. It is well established that blood pressure increases with obesity [52] and, conversely, that hypertension is a common complication of obesity.[53]

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52. Symonds, B.: The Blood Pressure of Healthy Men and Women, J. A. M. A. **80**: 232 (Jan. 27) 1923.
53. Terry, A. H., Jr.: Obesity and Hypertension, J. A. M. A. **81**: 1283 (Oct. 13) 1923.

The rational, practical concept of obesity so well summarized by Newburgh and Conn [54] is worth the careful consideration of every physician. Obesity in any circumstance represents the end result of a period of positive energy balance. Correction of obesity is achieved by reversal of this balance, whether by reduction in energy input or increase in energy output. Correction of biochemical lesions (resulting from endocrine disorders, for example) which influence the over-all energy exchange are correlative procedures. The devastation which obesity produces as reflected in life expectancy statistics is well established. More than any other group of diseases, cardiovascular disease is augmented by the complication of obesity; for not only is the work of the heart increased by the mechanical load but evidence is pointing to biochemical factors which encourage vascular disease in obesity.

A recent development in the treatment of obesity has been the introduction of the dextrorotatory isomer of amphetamine. It had previously been observed that *l*-amphetamine sulfate when given orally led to a diminution of appetite and loss of weight. The *d*-amphetamine sulfate is reputed to be more effective and less toxic. Gelvin and McGavack [55] studied this drug as an adjunct to therapy of obesity and found that, although an initial weight reduction could be effected, the weight loss was temporary and a plateau would soon be reached. Further study is needed, but at present it seems most probable that reduction of weight will depend on restriction of voluntary intake by more overt means.

Although some evidence has been obtained indicating usefulness of B complex vitamins in the treatment of myocardial infarction,[56] this therapy is not established. The use of the Karell diet (nothing but 800 cc. of milk per day) in the emergency phases of congestive failure is based on practicality. This diet is an interesting example of an empiric choice designed to accomplish limitation of calories and salt with palatability. This milk diet should not be continued for more than a few days unless supplemented with iron, thiamine, nicotinic acid and ascorbic acid and larger quantities of milk are used. The sodium content of milk is 0.047 Gm. per hundred milliliters. When the patient's appetite returns, a more adequate diet may be planned with restriction of salt and calories as necessary and with more liberal water and vitamin content.

A recent dietary treatment of hypertension which has received considerable acclaim is the "rice diet." [57] It is well to point out that this diet is nutritionally inadequate, particularly with respect to protein and vitamin content. The unpalatability of the diet often leads to caloric deficiency. We are inclined to believe that such efficacy of the diet in reducing blood pressure as is observed is primarily due to the low salt content coupled with a caloric deficit and consequent weight reduction. Master and his co-workers [58] have described the salutary effect of undernutrition and weight loss on cardiac output and blood pressure. There is no evidence that rice contains a blood pressure–lowering principle. Animal experimentation has confirmed only that the diet leads to inanition and moderate reduction of the blood pressure in dogs.[59]

A recent report [60] of the results obtained in a group of hypertensive patients using a low sodium (0.2 Gm. per day) diet, otherwise nutritionally sound, confirms the value of sodium restriction in the treatment of hypertension which may prove to be of greater value than sympathectomy.

NUTRITIONAL NEEDS IN INFECTIOUS DISEASES

It is a common belief that "malnourished" persons fall easy prey to infectious disease; yet there is little strictly objective evidence to support this belief. At present our knowledge is limited to the generality that host "resistance" is reduced by malnutrition.

Cannon [61] commented that, since the immune bodies of the serum are identified as globulins, a deficiency of diet protein may lead to impairment of antibody production. The experimental evidence to support this contention is based on the response of rats in a state of extreme protein deficiency. It remains to be shown whether the more chronic protein deficiency state seen in man leads to similar changes. Other workers have been unable to demonstrate an alteration of resistance to natural infections by dietary protein deficiency of less extreme degrees in the rat.[62] Recently Schneider [63] summarized experience with diet and resistance to infection in mice. It is concluded that there is a demonstrable influence of diet on host resistance under certain conditions. The nature of this relationship is yet little understood, so that it is not possible to make clinical applications. The effect of diet on resistance would seem to be more subtle than manifest by alteration of circulating antibodies.

Perhaps the most striking clinical evidence of the effect of nutrition on the course of an infectious disease is reflected in the remarkable fall of morbidity and mortality rates of typhoid fever after the starvation regimen of therapy was replaced by nutritionally adequate diets. A recent report [64] emphasized the importance of encouraging high caloric, high protein diets during convalescence from infectious disease. The problems of anorexia, nausea and vomiting can often be surmounted by education and explanation to the patient that the diet is medical treatment for the disease. The low calory concentration of conventional liquid diets often defeats the purpose of a liquid diet regimen.

Despite the clinical observations that convalescence in several infectious diseases is hastened by adequate diet, the classic study of Grossman and his co-workers [65] using the nitrogen balance technic indicates that a large negative nitrogen balance occurs with acute infectious diseases and that this wastage persists despite high

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protein and caloric intake. The nature of this phenomenon is not understood. The anemia of infection described by Cartwright and his co-workers,[66] in which anemia develops despite iron supplementation, seems to be a related phenomenon. The report of Croft and Peters [67] that the nitrogen wastage after thermal burns in rats could be significantly reduced by increases of dietary protein or by inclusion of 1 per cent of methionine suggests again that the limiting factor in convalescence may be one or a few essential substances.

There is little quantitative evidence concerning the effect of fever on vitamin requirements. Experimental evidence in rats,[68] which seems to indicate that thiamine, pyridoxine and choline requirements are increased by an increase of environmental temperature, has not been completely elucidated. Perhaps the best support for the inclusion of supplementary vitamins in the therapy of patients with infectious disease is the frequent observation that the florid deficiency states are often precipitated by an infectious disease. Classic beriberi or pellagra are frequently seen as a complication of an infectious disease occurring in a previously malnourished person.

Of interest in a discussion of the relationship of diet to "resistance" are the observations that inanition or thiamine deficiency appear to improve the resistance of experimental animals to virus infections or virus-incited tumors.[69] There is no evidence to support the contention that administration of any or all of the vitamins to previously well nourished persons will increase "resistance" to infection.

NUTRITIONAL NEEDS IN ENDOCRINE DISEASES

The treatment of diabetes mellitus is based on diet regulation. The immediate objectives of diet therapy in diabetes are: (1) to insure adequate nutrition, (2) to conserve the limited insulin-producing mechanism which remains and (3) to complement the regulation achieved with insulin.

Although there has been considerable clinical and experimental study of this subject, there is no conclusive evidence to support the contention that diabetics have increased requirements for B complex vitamins; and this despite the frequence of peripheral neuritis in diabetics which simulates a thiamine deficiency neuritis but which is more likely related to the inevitable progression of peripheral vascular disease.

The insurance of a nutritionally sound diet for diabetic persons almost certainly follows when diet therapy directed toward management of the endocrine disorder is commenced. The avoidance of concentrated carbohydrate foods, the use of leafy vegetables, fruits and whole grain cereals with daily servings of meat and eggs furnish a sound diet. Probably the most vulnerable aspect of the diet is its calcium content. A pint of milk daily should be a minimum allowance. As in patients with ulcer, diabetics should be taught the principles of diet selection and self management. When this task is well done, the diabetic person, as Joslin has pointed out, "is better off for his diabetes."

The protein requirements of persons with diabetes are not known to be abnormal so long as glycosuria is controlled. The National Research Council allowances for protein are adequate for the diabetic person.

The most satisfactory level of fat in the diet is probably between 75 and 125 Gm. per day, although some workers, notably Rabinowitch,[70] believe that a low fat diet will delay and minimize the vascular sclerosis so characteristic of diabetes. An average diet used by the Joslin group would contain 165 Gm. carbohydrate, 83 Gm. of protein and 97 Gm. of fat. This diet represents a conservative and probably the most widely used type of diet therapy in diabetes.

A relatively recent innovation and one which remains unevaluated is the "free diet" regimen introduced in 1932 [71] and in the past decade adopted by several clinics in this country. This procedure attempts to prevent acidosis by using insulin without dietary restriction. It has been particularly recommended for children when diet regulation may lead to psychiatric problems. The narrow margin of safety from coma, the persistent diuresis with consequent loss of electrolytes and calories and the potentially harmful effects of persistent hyperglycemia are all criticisms which may apply to this procedure. Clinical evaluation will require many years of careful study.

HYPERTHYROIDISM

The treatment of hyperthyroidism is directed toward correction of the metabolic defect. Until the excessive rate of metabolism can be controlled, either by chemotherapy or surgery or a combination of these procedures, the principal dietary problem is one of supplying sufficient calories so that the body stores will not be drawn on. High calory diets are indicated. Carbohydrate and fat supplements to a normal protein allowance must be assured. Often 5,000 to 6,000 calories may be necessary. In so far as the caloric requirement is not met, the dietary protein and body protein will be diverted to energy channels and a protein deficiency state with loss of weight will ensue. The evidence for increased vitamin requirement in hyperthyroidism is based on animal experimentation, principally with thiamine, which indicates that thiamine requirements are related to total caloric exchange.

It has been reported that liver feeding alleviates experimental thyrotoxicosis in rats.[72] The discovery of vitamin B_{12} led Nichol and his associates [73] to use vitamin B_{12} in place of liver. It was found that this new vitamin protected thyrotoxic animals as well as did liver and other crude materials, thus suggesting another possible clinical application of this new vitamin. Supplementary levels of B complex vitamins are indicated in thyrotoxicosis. There is no evidence pertinent to fat-soluble vitamin requirements.

CONCLUSION

A consideration of nutrition in illness and disease is important from the viewpoints of etiology, diagnosis, therapy and prevention. In our opinion nutrition is the most important single environmental factor affecting health.

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SATURDAY, FEBRUARY 11, 1950

ENROLMENTS IN MEDICAL SCHOOLS

In recent discussions concerning the supply of physicians some critics of the present methods of training have compared the number of medical students enrolled in the medical schools in the United States today with the number enrolled in 1905, the first year for which accurate data for student enrolments are available. They claim that today's enrolment is smaller. While the American Medical Association, the Association of American Medical Colleges and others concerned with medical education have pointed out repeatedly that many of the medical students of the earlier period were enrolled in substandard schools and could not therefore be considered the equivalent of medical students in the present day approved schools, quantitative studies on this point have not been made until recently.

The Council on Medical Education and Hospitals of the American Medical Association has just made a study to determine the comparative enrolments in approved medical schools during the 40 years since 1910, when the Council published its first list of approved medical schools. This study reveals that in 1910 there were 66 class A medical schools with a total enrolment of 12,530 students; in 1920 there were 70 class A medical schools with a total enrolment of 12,559 students; in 1930 there were 76 approved medical schools with a total enrolment of 21,597; in 1940 there were 77 approved medical schools with a total enrolment of 21,271; in 1950 there are 79 approved medical schools with an estimated total enrolment of 24,800 students. These data clearly show the opportunities to study medicine in approved medical schools have practically doubled in the last 40 years and have more than kept pace with the growth in population.

The number of physicians per 100,000 population in the United States declined from 149 in 1909 to 125 in 1929. Since 1929 the ratio has steadily risen to 137 in 1949. These new data showing the increasing number of students enrolled in approved medical schools reveal clearly that the decline in the physician-population ratio from 1909 to 1929 was due entirely to the closing of substandard medical schools. A physician-population ratio that included only physicians who were graduated from approved medical schools would reveal a steadily rising trend in the past four decades.

Even the poorest of the approved medical schools today have better staffs and facilities than most of the approved medical schools of 30 or 40 years ago, and the leadership of the medical profession and the medical colleges has resulted in the training of a greatly increased number of well qualified physicians to serve the American people. This accomplishment is important in the increasing life expectancy. In the last 40 years life expectancy at birth in the United States has increased more than 17 years. This accomplishment also is important in the reduction of maternal mortality, which in the last 20 years has been reduced by more than 85 per cent, and has influenced considerably the over-all crude death rate for the nation, which has shown a gradual decrease despite the aging of the population.

The general health of the population of the United States is constantly improving. No one can deny this without resorting to falsification. Those who claim that a health crisis exists in this country cannot prove it, and yet by inference, and often more directly, they plead a crisis to bolster their arguments for enlargement of medical schools and increase in enrolments of students. The latest report from the Council on Medical Education offers a convincing reply to those who doubt the effectiveness of the present orderly progression in medical education to meet the health needs of the nation. To heed the pleas of those who would discard order for chaos would cause a farrago that would return the level of medical education and care to that of several decades ago.

TREATMENT OF ALCOHOLISM WITH TETRAETHYLTHIURAMDISULFIDE

In 1914 Koelsch reported that workers who handled cyanamide experienced flushing of the face, headache, accelerated and deepened respiration and pulse rate and a feeling of giddiness on taking even a small amount of alcohol. Hald, Jacobsen and Larsen [1] discovered that tetraethylthiuramdisulfide is capable of producing the same symptoms after ingestion of alcohol. These observations suggested the use of this substance in the treatment of alcoholism. Antabus and other proprietary names have been applied to this agent.

Clinical application of antabus in the treatment of alcoholic addiction was first made in Denmark by Jacobsen and Martensen-Larsen.[2] They reported that

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the intake of alcohol by a person who has taken antabus twelve hours previously is followed after five to fifteen minutes by a feeling of heat in the face and intense vasodilatation in the face and neck. Vasodilatation in the scleras and slight edema under the lower eyelids are particularly characterisic. The vasodilatation is accompanied with corresponding increase in skin temperature in this area. The pulse rate is increased up to 140. The blood pressure is unaltered or slightly depressed. The cardiac output is increased about 50 per cent in resting persons and only slightly in persons doing moderate muscular work. The ventilation is increased with a corresponding decrease in alveolar carbon dioxide. Nausea usually begins thirty to sixty minutes after the intake of alcohol. The intense flushing disappears and is followed by facial pallor and a fall in systolic and diastolic blood pressures. Copious vomiting may occur. High doses of alcohol may result in dizziness and temporary unconsciousness. The subjective feelings are an intense feeling of discomfort, a pulsating headache, palpitation and dyspnea. The discomfort is so intense that, once experienced, it prevents the majority of patients from further attempts to take alcohol as long as they are using antabus.

The reaction to alcohol in patients prepared for treatment with antabus is believed to be due to increase in the blood of acetaldehyde, which is formed by some unknown reaction of the drug on the enzymes oxidizing alcohol in the organism. Acetaldehyde is regarded as a normal intermediate product in carbohydrate metabolism. An increased amount of this substance is found in the blood during ingestion of alcohol. Hald and Jacobsen [3] demonstrated a much higher concentration of acetaldehyde in the blood of persons treated with antabus after ingestion of alcohol. They also isolated and identified acetaldehyde chemically in increased amounts from the air exhaled by such persons. Identical symptoms could be elicited by intravenous injection in human beings of acetaldehyde.

The hypersensitivity to alcohol generally begins three to four hours after the ingestion of a single dose of alcohol and is fully developed during the next twenty-four hours. Jacobsen and Martensen-Larsen treated 550 alcoholics with antabus and reported a follow-up of three to six months of 50 patients. The dose was 1 to 2 Gm. on the first day and 0.75 to 1 Gm. on the next two days and thereafter 0.06 to 0.75 Gm. administered daily. This dosage was found to be at times inadequate. The authors then increased it to 2 Gm. the first day and 0.75 to 1 Gm. the following two days. The dose depends on the individual person and is adjusted so that the flushing occurs after 5 Gm. of alcohol is ingested. After three days of preparation the patient was asked to drink as he was accustomed to. Convulsions were seen in a few patients and were considered to be due to intense hyperventilation.

Jacobsen and Martensen-Larsen emphasize that it is essential in the treatment that the patient continue regular intake of the drug for some time. They also point out that, while a number of patients under treatment develop an aversion for alcohol sufficient to correct the habit, most patients require intensive psychotherapy for their mental and social rehabilitation. Group therapy, membership in "Ring i Ring," the equivalent of Alcoholics Anonymous, is recommended. Administration of vitamin B preparations and, in some cases, of insulin also has been reported valuable in physical rehabilitation.

The clinical experience so far has not been sufficient to indicate how long the patients must continue medication. Of the 99 persons treated by these authors and observed for six months or more, 52 can be regarded as socially recovered and 19 as being much better. Gelbman and Epstein,[4] in Canada, treated 55 patients; 45 patients did not revert to the drinking habit, while treatment failed in 10. Bell and Smith [5] treated 7 patients and came to the same conclusions as Jacobsen and Martensen-Larsen. They warn that antabus should not be given to a person under the influence of alcohol. Jones [6] reports the death of a healthy man aged 29 following a reaction which resulted from his taking 1 ounce (30 cc.) of rum after sensitization with antabus. He had received 5.5 Gm. of the drug before taking alcohol. The reaction observed over the two hours following the ingestion of alcohol was moderately severe. The reaction apparently had begun to subside, and the patient appeared to be in the sleepy stage, when, two and a half hours later, respiration ceased. Necropsy revealed acute congestive right-sided cardiac failure as the cause of death but gave no indication as to why cardiac failure should have occurred. Chemical analysis of the blood revealed a high level of acetaldehyde.

It is apparent that treatment of alcoholism with antabus is far from being free from danger. It should be carried out only in the hospital with small doses of both the drug and alcohol and with all the facilities at hand for emergency resuscitation. The patient should be carefully observed for a number of hours after the acute reaction.

A definite opinion as to the value and safety of antabus therapy of alcoholism must await more extensive and longer clinical observation. In the United States the drug is not available except for experimental investigation. Nor should it be made available until its true usefulness is determined and precautions are

3. Hald, J., and Jacobsen, E.: The Formation of Acetaldehyde in the Organism After Ingestion of Antabuse (Tetraethylthiuramdisulphide) and Alcohol, Acta pharmacol. et toxicol. 4:305, 1948.

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5. Bell, R. G., and Smith, H. W.: Preliminary Report on Clinical Trials of Antabuse, Canad. M. A. J. 60:286 (March) 1949.

6. Jones, R. O.: Death Following the Ingestion of Alcohol in an Antabuse Treated Patient, Canad. M. A. J. 60:609 (June) 1949.

taken to minimize the possibility of misuse. Improperly used this drug can be dangerous. In fact, even under carefully controlled conditions the drug must be used with extreme caution.

Current Comment

USE OF TELEVISION BY LOCAL MEDICAL SOCIETIES

Evidence of how local medical societies can promote public understanding and appreciation of their activities through the medium of television is presented in a report received from Mr. James O. Kelley, executive secretary of the Milwaukee Medical Society of Milwaukee County, Wisconsin. Chosen as one of thirteen outstanding state organizations deserving special mention in a television series presented weekly by the Marine National Exchange Bank of Milwaukee, the society was given a half-hour period for an interpretive review of its contributions to the community. To illustrate how much can be covered in a relatively short period if adequate attention is given to program outlining, Mr. Kelley and other representatives of the society were interviewed on the wide range of that organization's activities, including principles of medical service and ethics, with demonstration of how emergency medical calls are handled, the local Blue Cross and Blue Shield facilities, a special budget assistance plan worked out by the society for families or individuals not using established plans, the local cancer detection center, the diabetes detection program and poliomyelitis consultation services, with emphasis throughout on the basic motivation of community interest and service. This example should serve as a stimulus to development of similar programs in many localities where television facilities are available or are being developed.

ANTITREPONEMAL EFFECT OF CHLORAMPHENICOL

In 1948 the treponemicidal action of chloramphenicol was reported by Smith [1] and his associates after studies on experimentally induced syphilis in rabbits. After oral administration of 50 to 100 mg. of chloramphenicol per kilogram of body weight the syphilitic lesions became temporarily free of spirochetes. With this dosage as a guide, Romansky [2] and his associates of George Washington University and the Bureau of Venereal Disease, Washington, D. C., tested the therapeutic effects of the drug on 32 patients with early syphilis. Patients with lesions containing numerous Treponema pallidum were selected for this study. One group of patients received a daily oral dose of 120 mg. per kilogram of body weight. This was given in six equally divided doses at four hour intervals and continued for six days. Other groups were given daily doses of 60 mg. and 30 mg. per kilogram of body weight for four to eight days. With the 30 mg. dose spirochetes could not be demonstrated in the dark field by the end of twenty-two to twenty-eight hours. Healing of the syphilitic lesions was recorded by the end of the four to eight day period. In a typical case the Eagle flocculation titer was reduced from 1:512 to 1:8 by the end of a three month convalescent period. The only toxic or untoward reactions noted with the selected doses were occasional mild diarrhea and dryness of the mouth. The Jarisch-Herxheimer reaction was less frequent and less severe than that observed in syphilitic patients treated with penicillin. With penicillin the initial healing is at the periphery of the syphilitic lesion. With chloramphenicol the healing apparently is initiated at the base. One patient with late extensive gummas of the leg had a dramatic healing response within four days after beginning the treatment. Later stages of syphilis are now under investigation. Obviously further investigations are in order to determine the usefulness of this newer treatment. The procedure cannot at this time be recommended for other than experimental purposes.

1. Smith, R. M., and others: J. Bact. 55:425 (March) 1948.
2. Romansky, M. J.; Olansky, S.; Taggart, S. R., and Robin, E. D.: Science 110:639 (Dec. 9) 1949.

PSYCHOSOMATIC TOOTH DECAY

From clinical observations Mellars,[1] Miller [2] and others have suggested that numerous pathologic oral conditions may be due to psychosomatic factors. To test this theory Manhold [3] and his associates of the Department of Oral Pathology, Tufts College, Boston, made a comparison of the relationship between neurotic tendencies and dental caries in 49 students, faculty members and employees of his college. Each person was tested according to Bernreuter's [4] personality inventory technic and assigned scores varying from 0 to 100 on his neurotic scale. There were also recorded the DMF (decayed, missing, filled) dental scores. Among the 49 subjects, 28 were below the lowest level of neurotic tendencies, scoring 60 per cent or less on the Bernreuter scale. Of these, 24, or 85 per cent, had gained less than a 40 DMF score. Of the 21 subjects with neurotic tendencies (or Bernreuter percentages above 60) 16, or 76 per cent, had DMF scores above 40. High neurotic tendencies were thus correlated with high DMF scores and subneurotic tendencies with low DMF scores. A similar correlation was noted with Bernreuter's introversion-extroversion scores, 78 per cent of those with high scores showing DMF scores above 40 while 84 per cent of those with low scores showed DMF scores below 40. There appears to be a significant correlation between psychologic factors and dental caries, but the subject merits further investigation with different types and a larger number of subjects.

1. Mellars, N., and Herms, F. W.: Am. J. Orthodontics 32:30, 1946.
2. Miller, S. C., and Firestone, J. M.: Am. J. Orthodontics 33:675, 1947.
3. Manhold, J. H., and Manhold, V. W.: Science 110:385 (Dec. 2) 1949.
4. Bernreuter, R. G.: The Personality Inventory, Stanford University, California, Stanford University Press, 1935.

ORGANIZATION SECTION

THE PHYSICIAN'S FEDERAL INCOME TAX

Prepared by the Bureau of Legal Medicine and Legislation, American Medical Association

Federal income taxpayers on a calendar year basis must on or before March 15 do two things: (1) They must file their final returns for the year 1949 and (2) they must file a declaration of estimated tax for 1950.

Prior federal income taxpayers have already received from the appropriate office of the Collector of Internal Revenue necessary forms for the filing of the return and the declaration. They have also received copies of a small booklet prepared by the Treasury Department containing instructions to aid taxpayers in completing Form 1040A, Short Form 1040 and Long Form 1040, one of which most physicians will find suitable for their needs. Physicians who will make returns or file estimates for the first time can obtain copies of the necessary forms and of the booklet from the local office of the Collector of Internal Revenue.

GROSS INCOME

A physician's gross income is the total amount of money received by him during the year for professional services, regardless of the time when the services were rendered for which the money was paid, assuming that the return is on a cash receipts and disbursements basis, plus such money as he has received from investments and from other sources.

If a physician receives a salary as compensation for services rendered and in addition thereto living quarters or meals, the value to the physician of the quarters and meals so furnished ordinarily constitutes income subject to tax. If, however, living quarters or meals are furnished for the convenience of the employer, the value thereof need not be computed and added to the compensation otherwise received by the physician. As a general rule, the test of "convenience of the employer" is satisfied if living quarters or meals are furnished to a physician who is required to accept such quarters and meals in order to perform properly his duties. For example, if a physician employed by a hospital is subject to immediate service at any time during the twenty-four hours of the day and therefore cannot obtain quarters or meals elsewhere without material interference with his duties and on that account is required by the hospital to accept the quarters or meals furnished by it, the value thereof need not be included in the gross income of the physician.

Tuition payments and subsistence allowances for veterans made under the G. I. Bill of Rights are not taxable income.

DEDUCTIONS FOR PROFESSIONAL EXPENSES

A physician is entitled to deduct all current expenses necessary in carrying on his practice. The taxpayer should make no claim for the deduction of expenses unless he is prepared to prove the expenditure by competent evidence. As far as practicable, accurate itemized records should be kept of expenses and substantiating evidence should be carefully preserved. The following statement shows what such deductible expenses are and how they are to be computed:

Office Rent.—Office rent is deductible. If a physician rents an office for professional purposes alone, the entire rent may be deducted. If he rents a building or apartment for use as a residence as well as for office purposes, he may deduct a part of the rental fairly proportionate to the amount of space used for professional purposes. If the physician occasionally sees a patient in such dwelling house or apartment, he may not, however, deduct any part of the rent of such house or apartment as professional expense; to entitle him to such a deduction he must have an office there, with regular office hours. If a physician owns the building in which his office is located, he cannot charge himself with "rent" and deduct the amount so charged.

Office Maintenance.—Expenditures for office maintenance, as for heating, lighting, telephone service and the services of attendants, are deductible.

Supplies.—Payments for supplies for professional use are deductible. Supplies may be fairly described as articles consumed in the using; for instance, dressings, clinical thermometers, drugs and chemicals. Professional journals may be classified as supplies and the subscription price deducted. Amounts currently expended for books, furniture and professional instruments and equipment, "the useful life of which is short," generally less than one year, may be deducted, but if such articles have a more or less permanent value, their purchase price is a capital expenditure and is not deductible.

Equipment.—Equipment comprises property of a more or less permanent nature. It may ultimately wear out, deteriorate or become obsolete, but it is not the ordinary sense of the word "consumed in the using."

The cost of equipment such as has been described, for professional use, cannot be deducted as expense in the year acquired. Examples of this class of property are automobiles, office furniture, medical, surgical and laboratory equipment of more or less permanent nature, and instruments and appliances constituting a part of the physician's professional outfit, to be used over a considerable period of time, generally over one year. Books of more or less permanent nature are regarded as equipment, and the purchase price is therefore not deductible.

Although the cost of such equipment is not deductible in the year acquired, nevertheless it may be recovered through depreciation deductions taken year by year over its useful life, as described later.

No hard and fast rule can be laid down as to what part of the cost of equipment is deductible each year as depreciation. The amount depends to some extent on the nature of the property and on the extent and character of its use. The length of its useful life should be the primary consideration. The most that can be done is to suggest certain average or normal rates of depreciation for each of several classes of articles and to leave to the taxpayer the modification of the suggested rates as the circumstances of his particular case may dictate. As fair, normal or average rates of depreciation, the following have been suggested: automobiles, 25 per cent a year; ordinary medical libraries, x-ray equipment, physical therapy equipment, electrical sterilizers, surgical instruments and diagnostic apparatus, 10 per cent a year; office furniture, 5 per cent a year.

The principle governing the determination of all rates of depreciation is that the total amount claimed by the taxpayer as depreciation during the life of the article, plus the salvage value of the article at the end of its useful life, shall not be greater than its purchase price. The physician must in good faith use his best judgment and claim only such allowance for depreciation as the facts justify. The estimate of useful life, on which the rate of depreciation is based, should be carefully considered in each case.

Dues.—Dues paid to societies of a strictly professional nature are deductible. Dues paid to social organizations, even though their membership is limited to physicians, are generally held to constitute personal expenses and as such are not deductible. If, however, membership in social organizations, such as a country club, is maintained both for personal and professional or business purposes and if evidence can be produced to substantiate the claim that a part of the expenses of such membership was incurred for business purposes, then it would seem

that these latter expenses would be deductible. Further discussion of this particular aspect of the federal law will be found in a subsequent paragraph dealing with the deductibility of entertainment expenses.

The assessment, or nonrecurring dues, levied pursuant to a resolution adopted by the House of Delegates in 1948 on members of the Association was authorized by the constitution of the Association. Its payment was made mandatory by the by-laws. The payment of the assessment, or dues, would therefore seem to constitute an ordinary and necessary business expense within the meaning of section 23 (*a*) (1) *A* of the Internal Revenue Code. A categorical statement with respect to the matter cannot now be made, but an application is pending in the Office of the Commissioner of Internal Revenue for a definite ruling.

Postgraduate Study.—The Commissioner of Internal Revenue holds that the expense of postgraduate study is not deductible.

Traveling Expenses.—Traveling expenses, including amounts paid for transportation, meals and lodging, necessarily incurred in professional visits to patients and in attending medical meetings for a professional purpose, are deductible.

Entertainment Expenses.—The deductibility of entertainment expenses, when incurred for business purposes, has been upheld, as applied to an actor, in the case of *Blakmer v. Commissioner*, 70 F. (2d) 255. In the case of *Jacobson*, 6 T.C. 1048, the taxpayer was allowed a deduction of expenses incurred for entertaining clients and employees of his law firm. The deductibility of such expenses by an attorney came before the U. S. Tax Court in the case of *Clyde A. Armstrong v. Commissioner*, decided Aug. 29, 1947, 6 TCM 997. In a memorandum opinion rendered by Judge Opper, this was said:

> Taxpayer, a Pittsburgh attorney, became a member of the University Club and the Duquesne Club in order to have available facilities for the entertainment of his clients; his purpose in joining the clubs was not particularly to make contacts productive of new business. In 1942, 1943 and 1944 the Commissioner disallowed deductions representing club dues, but allowed 50 per cent of the house bills incurred by taxpayer at each of the clubs during those years. The court finds that taxpayer used the club facilities not less than 50 per cent of the time for entertaining clients and other purposes incident to the practice of his profession, and allows the deduction of dues to that extent.

In the December 1948 issue of the *Medical Annals of the District of Columbia*, page 697, there was published correspondence that had passed between the secretary of the Medical Society of the District of Columbia and the Internal Revenue Agent in the Baltimore Division, Treasury Department, in which the latter stated that if entertainment expenses incurred by a physician have a direct relation to the production of income, and can be supported by the taxpayer, they will be taken into consideration in determining his net taxable income.

Automobiles.—Payment for an automobile is a payment for permanent equipment and is not deductible. The cost of operation and repair, and loss through depreciation, are deductible. The cost of operation and repair includes the cost of gasoline, oil, tires, insurance, repairs, garage rental (when the garage is not owned by the physician), chauffeur's wages and the like.

Deductible loss through depreciation of an automobile is the actual diminution in value resulting from obsolescence and use and from accidental injury against which the physician is not insured. If depreciation is computed on the basis of the average loss during a series of years, the series must extend over the entire estimated life of the car, not merely over the period in which the car is possessed by the present taxpayer.

If an automobile is used for professional and also for personal purposes—as when used by the physician partly for recreation, or so used by his family—only so much of the expense as arises out of the use for professional purposes may be deducted. A physician doing an exclusive office practice and using his car merely to go to and from his office cannot deduct depreciation or operating expenses; he is regarded as using his car for his personal convenience and not as a means of gaining a livelihood. What has been said in respect to automobiles applies with equal force to horses and vehicles and the equipment incident to their use.

Surgical Uniforms.—Amounts expended by surgeons for the purchase and maintenance of distinctive types of uniforms which are not adaptable to ordinary wear and which are required to be worn while on duty are deductible as ordinary and necessary business expenses.

MISCELLANEOUS

Contributions to Charitable Organizations.—For detailed information with respect to the deductibility of charitable contributions generally, physicians should consult the official return blank or obtain information from the collectors of internal revenue or from other reliable sources. An individual taxpayer can deduct such contributions only to the extent that they do not exceed 15 per cent of his adjusted gross income. The physician may not deduct as a charitable contribution the value of services rendered an organization operated for charitable purposes.

Bad Debts.—Physicians who make their returns on a cash receipts and disbursements basis, as most physicians do, cannot claim deductions for bad debts.

Taxes.—Taxes generally, either federal or state, are deductible by the person on whom they are imposed by law. Both real and personal property taxes are deductible; but so-called taxes, more properly assessments, paid for local benefits, such as street, sidewalk and other like improvements, imposed because of and measured by some benefit inuring directly to the property against which the assessment is levied, do not constitute an allowable deduction from gross income. Physicians may deduct state gasoline taxes and state sales taxes. In some states sales taxes are imposed on the seller, but if they are passed on to the buyer the latter may deduct them.

State income and use taxes are deductible; federal income taxes are not. Federal import, excise or stamp taxes are deductible only to the extent that they are attributable to business activities. State automobile license fees are deductible. If a state or local fee is imposed for regulatory purposes, and not to raise revenue, the fee may not ordinarly be deducted as a tax. If such fees, however, are classifiable as a business expense they are deductible as such. Annual registration fees imposed on physicians probably come within the category of regulatory fees and should be deducted as a business expense rather than as taxes. Local and state occupational taxes imposed on physicians are deductible either as taxes or as a business expense, depending on the purpose for which the tax is imposed.

The excise taxes imposed on employers by section 804, title VIII, and section 901, title IX, of the Social Security Act, commonly referred to as old age and unemployment benefit taxes, are deductible annually by employers in computing net income for federal income tax purposes. If the taxpayer's return is made on a cash basis, as are the returns of practically all physicians, the taxes are deductible for the year in which they are actually paid. If the return is made on an accrual basis, the taxes are deductible for the year in which they accrue, irrespective of when they are actually paid. Employees, including physicians whose employment brings them within that category, may not deduct the tax imposed on them by section 801, title VIII, of the Social Security Act, generally referred to as the old age benefits tax. If, however, the employer assumes payment of the employee's tax and does not withhold the amount of the tax from the employee's wages, the amount of the tax so assumed may be deducted by the employer, not as a tax paid but as an ordinary business expense.

Medical Expense.—A taxpayer may deduct amounts expended for medical, dental and hospital expense for himself, his spouse or a dependent, not compensated for by insurance or otherwise, including amounts paid for health and accident insurance, according to a prescribed formula. The law limits the deduction to a maximum of (*a*) $1,250 if the taxpayer claims only one exemption; (*b*) $2,500 if the taxpayer is a single person or if married and filing a separate return and claims more than one exemption; (*c*) $2,500 if the taxpayers are married and file a joint

return and claim two exemptions, $3,750 if three exemptions are claimed and $5,000 if four or more exemptions are claimed.

Laboratory Expenses.—The deductibility of the expenses of establishing and maintaining laboratories is determined by the same principles that determine the deductibility of corresponding professional expenses. Laboratory rental and the expenses of laboratory equipment and supplies and of laboratory assistants are deductible when under corresponding circumstances they would be deductible if they related to a physician's office.

Losses by Fire or Other Causes.—Loss of and damage to a physician's equipment by fire, theft or other cause, not compensated by insurance or otherwise recoverable, may be computed as a business expense and is deductible, provided evidence of such loss or damage can be produced. Such loss or damage is deductible, however, only to the extent to which it has not been made good by repair and the cost of repair claimed as a deduction.

Insurance Premiums.—Premiums paid for insurance against professional losses are deductible. This includes insurance against damages for alleged malpractice, against liability for injuries by a physician's automobile while in use for professional purposes, and against loss from theft of professional equipment and damage to or loss of professional equipment by fire or otherwise. Under professional equipment is to be included any automobile belonging to the physician and used for strictly professional purposes.

Expense in Defending Malpractice Suits.—Expense incurred in the defense of a suit for malpractice is deductible as a business expense.

Sale of Spectacles.—Oculists who furnish spectacles, etc., may charge as income money received from such sales and deduct as an expense the cost of the article sold.

Coming Medical Meetings

Annual Congress on Industrial Health, New York, Roosevelt Hotel, Feb. 20-21. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago 10, Secretary.

American Academy for Cerebral Palsy, New York, Waldorf-Astoria Hotel, Feb. 16-17. Dr. Meyer A. Perlstein, 4745 N. Drake Ave., Chicago 25, Secretary.

American Academy of Allergy, Los Angeles, Hotel Biltmore, March 6-8. Dr. Theodore L. Squier, 208 E. Wisconsin Ave., Milwaukee 2, Secretary.

American Academy of General Practice, St. Louis, Kiel Auditorium, Feb. 20-23. Mr. Mac F. Cahal, 406 W. 34th St., Kansas City, Mo., Executive Secretary.

American Academy of Orthopedic Surgeons, New York, Waldorf-Astoria Hotel, Feb. 11-16. Dr. Harold B. Boyd, 869 Madison Ave., Memphis, Tenn., Secretary.

American Association of Anatomists, New Orleans, Louisiana State University, April 3-5. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

American Association of Railway Surgeons, Chicago, Drake Hotel, April 4-6. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

American Goiter Association, Houston, Texas, March 9-11. Dr. George C. Shivers, 100 E. St. Vrain St., Colorado Springs, Colo., Secretary.

Chicago Medical Society Annual Clinical Conference, Chicago, Palmer House, Feb. 28-March 3. Dr. H. Kenneth Scatliff, 30 N. Michigan Blvd., Chicago 2, Secretary.

Dallas Southern Clinical Society, Dallas, Texas, March 13-16. Miss Betty Elmer, 1133 Medical Arts Bldg., Dallas 1, Executive Secretary.

Michigan Postgraduate Clinical Institute, Detroit, Book-Cadillac Hotel, March 8-10. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing 8, Secretary.

Mid-Atlantic Section, American Urological Association, Hot Springs, Va., The Homestead, March 23-25. Dr. H. N. Dorman, 1025 Connecticut Ave, N. W., Washington 6, D. C.

Missouri State Medical Association, St. Louis, March 26-29. Dr. H. E. Petersen, 634 N. Grand Blvd., St. Louis 3, Secretary.

National Society for the Prevention of Blindness, Miami, Fla., Hotel Floridian, March 26-30. Dr. Franklin M. Foote, 1790 Broadway, New York 19, Executive Director.

New Orleans Graduate Medical Assembly, New Orleans, Municipal Auditorium, March 6-9. Dr. Woodard D. Beacham, 1430 Tulane Ave., New Orleans, Secretary.

Southeastern Allergy Association, Columbia, S. C., Columbia Hotel, Feb. 11-12. Dr. Katharine B. MacInnis, 1315 Bull St., Columbia 49, S. C., Secretary.

Southeastern Surgical Congress, Washington, D. C., March 6-9. Dr. Benjamin T. Beasley, 45 Edgewood Ave. S.E., Atlanta 3, Ga., Secretary.

Official Notes

THE CHARLES BRANT FUND

Through the Charles Brant Fund there are available the limited funds for the support of research in clinical medicine. Applications for aid may be forwarded to the office of the Council on Pharmacy and Chemistry in care of the American Medical Association. They should give full information about the research, proposed or under way, the working personnel and the available facilities.

Medical Legislation

STATE LEGISLATION

Georgia

Bills Introduced.—H. 876 proposes to amend the law relating to nurses' examinations by providing regulations for the examination and licensing of practical nurses. S. 126 proposes regulations for the chartering of nonprofit corporations organized for the purpose of establishing, maintaining and operating nonprofit hospital service plans.

Kentucky

Bills Introduced.—S. 56 proposes to make it unlawful to sell, dispense or furnish barbiturates except on the prescription of a practitioner which is defined to be a person licensed in the state to prescribe and administer barbiturates.

Massachusetts

Bills Introduced.—H. 948 proposes to authorize chiropodists and podiatrists to order or prescribe narcotic drugs under the provisions of the narcotic drug act. H. 958, to amend the law relating to the use of dead bodies for the promotion of anatomic science, proposes to include schools of chiropody along with medical schools in the list of institutions which may make use of such dead bodies. H. 1099 proposes the creation of a board of registration of physical therapists and defines physical therapy to mean the treatment of various conditions and diseases of the human body by the effective use of the physical properties of hydrotherapy, thermotherapy, phototherapy, electrotherapy and mechanotherapy. The proposal would also require that no person shall practice or attempt to practice physical therapy, or hold himself out as a physical therapist, or designate himself, or describe his occupation, by the use of any words or letters calculated to lead others to believe that he is a registered physical therapist, unless he has been registered within the provisions of the proposal. H. 1456 proposes the creation of an office of state physician to establish and administer health service programs for the employees of the commonwealth. H. 1457 proposes the creation of a board of registration of chiropractors and defines chiropractic as the science of locating and removing by hand adjustment only, interference with the transmission or expression of nerve force in the human body, by the correction of misalinement of subluxations of the vertebral column. It excludes operative surgery, prescription or use of drugs or medicine, or the practice of obstetrics, except that the x-ray and analytic instruments may be used solely for the purposes of examinations; chiropractor is defined as a person who lawfully practices chiropractic. H. 1610 proposes the creation of a special commission to make an investigation into the business affairs and practices of the Massachusetts School of Physiotherapy. H. 1695 proposes regulations for the establishment of a voluntary system for the payment of hospital, surgical operation, sickness, bodily injury and maternity benefits to employees. H. 1703 proposes the creation of a Massachusetts Cash Sickness Compensation Fund. H. 1720 proposes the creation of the position of director of animal experimentation and proposes regulations for the licensing, registration and inspection of laboratories, corporations, educational institutions and the like engaged in performing experiments, research observation or instruction using living animals. H. 1807 proposes an appropriation for the commonwealth to pay to hospitals having approved training schools for nurses the sum of $50 per month for each student nurse for each month she is in training so long as the school is approved. S. 393 and S. 393 propose that no person other than a licensed hairdresser operating a registered beauty shop shall sell or offer for sale or give away any cosmetic containing any harmful ingredient, which is defined to include ammonium hydroxide, thyoglycollic acid and formaldehyde.

Mississippi

Bills Introduced.—H. 399 proposes the establishment of a four year standard medical school as a part of the University of Mississippi. S. 230 proposes that all applicants for a marriage license shall present a certificate signed by an active licensed physician in Mississippi, or a physician licensed to practice in any of the other states or in the District of Columbia, indicating that the applicant has been given a general physical examination.

New Jersey

Bill Introduced.—A. J. RES. 1 proposes the creation of a commission to study the subject of providing the state of New Jersey with a medical school.

New York

Bills Introduced.—A. 828, 13 proposes that the legislature of the state of New York reiterate and confirm its opposition to the theory and practice of euthanasia in any form in the nation and especially in the state of New York. A. 354 and S. 347 propose the creation of a board of examiners of massage and define massage as the stroking, kneading, tapping or rolling with the hands, or with other instrumentalities, of the human body for hygienic or remedial purposes, for the purposes of relieving, alleviating or reducing affected parts thereof, but shall not include the reduction of a fracture or dislocation of a bone. A. 828, to amend the education law, proposes that the practice of roentgen diagnosis, roentgen treatment and radium treatment shall be deemed to be the practice of medicine. A. 899, to amend the public health law, proposes the creation in the state department of health of an adult hygiene and geriatrics division, designed to improve and protect the health and vitality of middle aged and elderly citizens of the state. A. 1000 proposes an appropriation of $1,000,000 to the department of health to defray the cost of research in the cause and cure of multiple sclerosis in order to control and prevent this disease. S. 435, to amend the public health law, proposes that the term physician shall include osteopathy when used with reference to narcotic drugs. S. 379, to amend the domestic relations law, proposes that a child born to a married woman by means of artificial insemination with the consent of her husband shall be deemed the legitimate, natural child of both the husband and wife for all purposes and such husband and wife and child shall sustain toward each other the legal relation of parent and child and shall have all the rights and be subject to all the duties of that relationship including the rights of inheritance from each other.

Virginia

Bills Introduced.—H. 66, S. 60 and S. 61 propose regulations amending the law relating to the granting of medical scholarships.

Washington Letter

(From a Special Correspondent)

Feb. 6, 1950.

Ewing Returns from Europe

The Federal Security Administrator, Oscar R. Ewing, disembarked in New York City on January 17, ending a six week tour of European countries and the Middle East to inspect national systems for medical care, education and social welfare. In a statement, prepared on shipboard en route home and issued two days later, he said, in part:

"Such partisan or selfish opposition as may develop (against the administration's 'Fair Deal' program) will receive its full come-uppance when the voters select an Eighty-Second Congress next fall. Aid to education, extension of social security, establishment of national health insurance and protection of civil rights are bound to come.

"I come home with even greater confidence in President Truman's proposal for national health insurance in the United States. His proposal is based on principles entirely different from those of the British program, which I investigated in some detail. The British plan is totally unsuited for the United States. In England the health service is part of a broad program to reorganize the basic social and economic structure of the country, and eight ninths of its costs come out of general tax revenues. This is utterly foreign to the President's proposal. His is strictly an insurance plan, on a pay-as-you-go actuarial basis, and intended solely to eliminate the dollar barrier between the average American and the medical care he needs. We seek only to solve the financial problems relating to medical care and leave all professional medical problems to the doctors."

Addressing the National Press Club in Washington January 26, Mr. Ewing stoutly denied that the administration's campaign for compulsory health insurance is a step toward socialization in government. The British and Swedish medical care systems "leave no doubt that their services are part of an over-all plan to nationalize all that can be nationalized," said Ewing. But the scheme proposed for this country, he explained, is totally different, in that it would be financed by payroll taxes on employers and employees, whereas eight ninths of the British plan's cost is paid for out of general funds.

Seated beside Administrator Ewing were the congressional champions of the Truman-Ewing health insurance bill, Senators Claude Pepper and James E. Murray and Representative Andrew Biemiller. In the audience were several members of Washington's medical profession, along with several hundred news writers and columnists.

Senator Hunt Introduces Health Bill

Senator Lester C. Hunt (Democrat, Wyoming) introduced his national health bill on January 30, a three part plan providing for establishment of a Department of Health, federal assistance to rural and "shortage" areas and operation of a modified health insurance system by the proposed department. Senator James E. Murray (Democrat, Montana), chairman of the Senate subcommittee on health legislation, intimated that his group will not conduct public hearings on the Hunt bill. The chairman is co-sponsor of the administration's bill for compulsory national health insurance.

Head of the Department of Health and a member of the President's Cabinet would be a "professional health worker," either a physician or dentist, who possessed "broad experience in the field of medical or dental education," by terms of the Hunt bill (S. 2940). Similar qualifications are specified for the Under Secretary of Health. Five assistant secretaries are provided to supervise a Bureau of Medical and Hospital Care, a Bureau of Public Health Practice, a Bureau of Children's Health, a Bureau of Research and a Bureau of Staff Services. The Department of Health would strip all health and medical activities from the existing Federal Security Agency, including Public Health Service and Food and Drug Administration in toto, plus health functions of the Children's Bureau, Social Security Administration and Office of Vocational Rehabilitation.

Title II of S. 2940, devoted to government special aid to regions deficient in medical and hospital personnel and facilities, authorizes loans and grants as an incentive to physicians and professional auxiliaries to settle and practice in these so-called shortage areas, to hospitals and health centers to defray operational expenses and to organizations sponsoring construction of hospitals. A separate section of Title II provides for federal grants to farmers' cooperatives "to initiate and carry out experimental plans for providing comprehensive medical care for their members as a means of demonstrating the practicality and effectiveness of such plans." For loans and grants under provisions of Title II, appropriations totaling $45,000,000 for the first year of operation are authorized.

Subscription to the health insurance plan would be voluntary and limited to individuals and families having incomes of $5,000 or less annually. Operation of the scheme is placed in control of a five member National Health Insurance Board, whose authority would be practically unlimited. The Surgeon General of Public Health Service would serve as chairman, with the President appointing the other four members—one each representing hospitals and dentistry and the other two from the public at large. The four appointees would serve full time at $15,000 annual salaries. No provision is made for states' participation in adoption of fee schedules, fixing of premium payments and the like, although the wording of the bill is such that cooperative effort is not precluded. All would depend on the wishes of the National Health Insurance Board.

President Supports Heart Disease Campaign

President Truman issued a special statement February 2 urging "every citizen to learn the facts about heart diseases and the steps that are being taken to combat them." His message was a part of the February annual fund-raising campaign sponsored by American Heart Association.

"Many of our finest scientific minds, our most highly skilled physicians, our civic-minded business and professional leaders are enlisted in this great crusade," said President Truman. "But they cannot be expected to do the whole job by themselves. Victory in the fight they are waging for all the people can be achieved only with the cooperation of the general public. I urge every citizen, for his own sake and that of the Nation as a whole, to give wholehearted support to physicians and scientists engaged in an unceasing battle against heart diseases."

GOVERNMENT SERVICES

NAVY

GRADUATE TRAINING

Among the 1,570 regular Navy medical officers on duty Jan. 1, 1950, certification by American Specialty Boards have been made by 208, and 30 others had completed a portion of their board examinations. The specialties in which certifications have been made are anesthesia 6, dermatology and syphilology 7, internal medicine 37, obstetrics and gynecology 15, ophthalmology 16, otolaryngology 25, orthopedics 16, pathology 13, pediatrics 8, plastic surgery 1, psychiatry and neurology 28, radiology 21, surgery 21, urology 11 and preventive medicine and public health 13. The trend toward specialization prompted the Bureau of Medicine and Surgery to institute a revised program of training in 1946 whereby naval medical officers could advance professionally and also gain recognition in their specialty. The goal of the Bureau of Medicine and Surgery is to further individual development so that the Medical Corps of the Navy will be maintained on a parity with the highest standards. Certification of naval medical officers is made possible through the combined resources of the Navy and many of the large civilian medical schools, medical centers and approved hospitals in every part of the United States.

A total of 265 medical officers in naval hospitals are in approved residency training, while 142 are in approved residency training in medical specialties in civilian hospitals throughout the United States and Europe. In addition to this group, 41 medical officers are taking special courses as follows: aviation medicine 26, submarine medicine 4, hospital administration 2, radiologic defense 4, research (radiobiologic) 1, biophysics (radiologic) 1 and service colleges 3.

142
50

PSYCHOLOGISTS WANTED

The following civil service positions are open to psychologists for placement in naval hospitals:

Clinical psychologist, U. S. Naval Hospital, Portsmouth, Va. (Civil Service, GS-11, $5,400 per annum). Consultative and diagnostic duties predominate; little research and no training. Experience and education: doctoral level with experience in medical setting required.

Chief clinical psychologist, Training and Research Center, Naval Hospital, Mare Island, Vallejo, Calif. (Civil Service GS-13, $7,600 per annum). Education and experience: Ph.D., administrative, research and training experience.

Clinical Psychologist (research) for Neuropsychiatric Treatment, Training and Research Center, Naval Hospital, Mare Island, Calif. (Civil Service GS-12, $6,400 per annum). Education and experience: Ph.D.; must also be capable of conducting research in dynamic psychology.

For information consult commanding officers of respective naval hospitals or the Bureau of Medicine and Surgery, Attn.: Professional Division, Navy Department, Washington 25, D. C.

DUTY UNDER INSTRUCTION

The following Navy medical officers have been nominated for duty under instruction in the Navy's Graduate Medical Training Program:

Comdr. William H. Gulledge, to a residency in children's orthopedics, Shriner's Hospital, Honolulu, Hawaii.

Comdr. William F. Queen, for instruction in basic science in internal medicine, Army Medical Center, Washington, D. C.

Lieut. James D. Hague, to a fellowship in psychiatry, University of Louisville School of Medicine, Louisville, Ky.

Lieut. Mervyn J. Sullivan, to a residency in obstetrics and gynecology, Naval Hospital, Long Beach, Calif.

Lieut. David J. Williams Jr., to a residency in surgery, Naval Hospital, Philadelphia.

Lieut. (jg) James R. Dineen, to a residency in orthopedics, Children's Hospital, Boston.

Lieut. (jg) Bernard D. Sherer, to a residency in surgery, Naval Hospital, Philadelphia.

Lieut. (jg) Herbert L. Walter, to a residency in internal medicine, Naval Hospital, St. Albans, L. I., N. Y.

NEW REGULAR OFFICERS

The following officers have been appointed to the regular Navy from an active reserve status:

Lieut. (jg) Willard P. Arentsen, Stratford, N. J.
Lieut. (jg) Maurice N. Johnson, Minneapolis.
Lieut. (jg) Richard H. Lee, Northfield, Minn.
Lieut. (jg) Donald J. MacPherson, Lynn, Mass.

PUBLIC HEALTH SERVICE

1,000 NEW HOSPITALS

The Edward John Noble Hospital, Canton, N. Y., became the thousandth hospital construction project to be approved for federal aid under the Hospital Survey and Construction Act. Construction of the 51 bed hospital, at an estimated cost of $525,000, will begin in the spring of 1950. The cost is being financed by a $175,000 contribution from the Edward John Noble Foundation, $175,000 by the citizens of the area which the new hospital will serve and $175,000 in federal funds, granted by the Public Health Service. Plans for the hospital were approved by the New York State Joint Survey and Planning Commission and the Public Health Service. The hospital is the third in a system of hospitals to be constructed in upstate New York, to be known as the "North Country Hospitals." Two additional units in the system are under construction at Gouverneur, N. Y., in St. Lawrence County and at Alexandria Bay, in Jefferson County, with construction costs to be financed by public subscription, a grant from the foundation and federal funds. The hospital at Gouverneur, which will have 60 beds and cost about $1,084,000, is expected to be completed by May 1950, and the hospital at Alexandria Bay, containing 30 beds and costing $437,000, by June.

The Edward John Noble Foundation was founded by Edward J. Noble, chairman of the board of the American Broadcasting System, for public service in the fields of education, health and religion.

REGULAR CORPS EXAMINATION FOR MEDICAL OFFICERS

A competitive examination for appointment of medical officers in the Regular Corps of the U. S. Public Health Service will be held May 15-17, 1950, at a number of points throughout the United States. Applications must be received no later than April 17.

The regular corps is a commissioned officer corps composed of members of various medical and scientific professions. Appointments will be made in the grades of assistant surgeon and senior assistant surgeon. All commissioned officers are appointed to the general service and are subject to change of station and assignment as necessitated by the needs of the service, although consideration is given to the officer's preference, ability and experience. Appointments are permanent and provide opportunities to qualified physicians for a life career in clinical medicine, research and public health.

Requirements are United States citizenship, at least 21 years of age and graduation from a recognized school of medicine. Assistant surgeon: At least seven years of educational training and professional experience subsequent to high school. Senior assistant surgeon: At least ten years of educational training and professional experience subsequent to high school.

Applicants who will complete these requirements within nine months of the date of the written examination will be admitted but may not be appointed until they meet the above requirements. Physicians successful in the examination and who are now serving internships will not be placed on active duty in the Regular Corps until completion of internship. The examination will include an oral interview, physical examination and written objective tests covering the professional field. The written professional examination will cover anatomy, physiology, biochemistry, microbiology and pathology; practice of medicine, including internal medicine, therapeutics and toxicology, pediatrics, obstetrics and gynecology, surgery, orthopedics, gynecology, and preventive medicine and public health.

Entrance pay for an assistant surgeon with dependents is $5,686.56 per annum; for senior assistant surgeon with dependents, $6,546. These figures include the $1,200 annual additional pay received by medical officers as well as subsistence and rental allowance. Provisions are made for promotion at regular intervals. Retirement pay after 30 years of service or at the age of 64 is three fourths of annual basic pay at the time of retirement.

STUDIES OF MULTIPLE SCLEROSIS

The National Institute of Mental Health has awarded $62,650 to Elvin A. Kabat, Ph.D., for immunochemical studies of multiple sclerosis and of experimental acute disseminated encephalomyelitis. The grant is for a two year study. Dr. Kabat is associate professor of bacteriology at Columbia University. He will continue studies on demyelinating diseases previously carried on under a grant from the National Multiple Sclerosis Society. He will also investigate the proteins in the cerebrospinal fluid to determine their relation to the clinical status of a patient with multiple sclerosis.

VETERANS ADMINISTRATION

HOME TOWN PHARMACY PROGRAM

The nation's retail pharmacists filled 641,000 prescriptions for veterans under the Veterans Administration "home town" pharmacy program during 1949, representing an increase of 141,000 over those filled in 1948. Under agreements between VA and state pharmaceutical associations in 44 states, the District of Columbia and Hawaii, private pharmacists have been authorized to fill prescriptions, at government expense, for veterans undergoing outpatient treatment for service-connected ailments in VA clinics or with private physicians. In addition to prescriptions filled by private druggists, 3,273,000 were filled during 1949 by the 262 pharmacists in VA hospitals and centers, and another 1,103,000 were filled by 112 pharmacists in VA regional offices.

NEW HOSPITAL IN PHILADELPHIA

The contract has been awarded for the construction of a 500 bed Veterans Administration hospital in Philadelphia on an 18 acre site near the University of Pennsylvania Medical School. In addition to the hospital building, the project consists of nurses' and attendants' quarters, an apartment building and other buildings, such as a laundry, boiler house and garage.

PERSONAL

Dr. Richard B. Bean has been promoted to chief medical officer of the Veterans Administration regional office in Buffalo, to succeed the late Dr. Frank Brundage. Dr. Bean is a former president of the Wyoming County (N. Y.) Medical Society.

MISCELLANEOUS

EXAMINATION TO FILL POSITIONS IN NEW ENGLAND

An examination will be held for filling the position of medical officer in various federal agencies in New England other than the Veterans Administration and the U. S. Public Health Service. The options in this examination include general practice, adjudicative medicine, administrative medicine, anesthesia, occupational health and medicine, pediatrics, physiology, psychiatry, and chest, general, orthopedic and plastic surgery. The grades for which the examination has been announced are compensated at entrance salaries of $5,400, $6,400 and $7,600 per annum. The vacancies represent a wide range of professional positions in the federal service. Preference in certification is given to residents of New England; however, an insufficient number of qualified medical officers have filed application to date. Applicants who wish to apply should submit Application Form 57 and 5001-ABC (obtainable at any first and second class post office) to the First U. S. Civil Service Regional Office, Boston 9, Mass., in order that they be received not later than Feb. 23, 1950.

SUMMER COURSES IN RADIOISOTOPE TECHNIC

The Oak Ridge Institute of Nuclear Studies will conduct basic radioisotope technics courses June 5-30, July 3-28 and July 31-August 25. Priority will go to university personnel who have difficulty attending courses during the winter. The courses are open to senior research personnel. Thirty-two participants will be accepted for each of the three repeated courses. Each session is comprised of laboratory work, lectures on laboratory experiments, general background lectures and special topic seminars. Experiments cover the use and calibration of instruments, purification and separation procedures and the application of radioisotope technics. Seminars include such discussions as the use of radioisotopes in animal and human experimentation, principles and practices of health-physics, design of radiochemical laboratories, dosimetry, instrumentation and radiation effects on cells. A registration fee of $25 is charged for the course. Dormitory or hotel facilities are available in Oak Ridge for participants. Information may be obtained from Dr. Ralph T. Overman, Chairman, Special Training Division, P. O. Box 117, Oak Ridge, Tenn.

DR. PEARSON APPOINTED CHIEF OF BIOLOGY BRANCH

Dr. Paul B. Pearson, who has been acting chief of the Biology Branch of the Division of Biology and Medicine, U. S. Atomic Energy Commission, has been appointed chief of the branch. Dr. Pearson formerly was dean of the graduate school and head of the Department of Biochemistry and Nutrition of the Agricultural and Mechanical College of Texas. He is a native of Utah and received his Ph.D. in biochemistry from the University of Wisconsin. The AEC also announced that Dr. M. R. Zelle, former professor of bacteriology at Cornell University, has joined the staff of the biology branch as geneticist. He served as a biologist with the National Institutes of Health, 1946 to 1948, as assistant professor of genetics at Purdue University and as a naval officer during World War II. Dr. Zelle, a native of Iowa, received his Ph.D. degree at Iowa State University.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ALABAMA

Cancer Seminar.—A three day seminar on cancer will be held at the Medical College of Alabama in Birmingham February 21-23. The program is as follows:

Louis H. Clerf, Philadelphia, Cancer of the Pharynx, Hypopharynx and Larynx.
Frank Adair, New York, Cancer of the Breast.
Oliver S. Moore, New York, Cancer of the Mouth.
Axel N. Arneson, St. Louis, Cancer of the Female Genital Organs.
Harry E. Bacon and Lloyd F. Sherman, Philadelphia, Cancer of the Colon and Rectum.
Sidney Farber, Boston, Lymphoblastomas.
Ralph M. Caulk, Washington, D. C., Radiation Therapy of Cancer of Pharynx and Larynx.
Alexander Brunschwig, New York, Cancer of the Stomach.

Dr. Charles S. Cameron Jr., New York, medical and scientific director of the American Cancer Society, will give the dinner address at 8:30 p. m. Reservations for the seminar should be made through Dr. Karl F. Kesmodel, Medical Arts Building, Birmingham.

CALIFORNIA

Course in Pediatrics.—The Southwestern Pediatric Society will present its postgraduate lecture course February 21-22 at the Biltmore Hotel, Los Angeles. Dr. Waldo E. Nelson, professor of pediatrics, Temple University School of Medicine, Philadelphia, and Dr. Clement A. Smith, director of the Laboratory for Research on Newborn, Boston, will be the speakers. At the dinner meeting Wednesday Dr. Nelson will speak on "The Role of the Practitioner in Clinical Investigation." The course is open to all physicians, and the registration fee of $15 includes the dinner. Checks for reservations, which must be received before February 18, may be made payable to the Southwestern Pediatric Society Postgraduate Course, 10711 Riverside Drive, North Hollywood.

Diphtheria in San Francisco.—The San Francisco Department of Public Health reports that the number of local cases reported for 1949 was 78. Except for 1948 the incidence in 1949 was the highest since 1933. The fatality rate remained about the same as for 1948. Diphtheria in San Francisco is definitely a disease of adults. Forty-six per cent of the cases occurred in age groups over 40 with 16 per cent of them in the 45-49 group. In the younger age groups the highest percentage of cases was in the under 5 group and in the 30-34 group. The record for 1949 shows 17 per cent of the patients immunized, compared with 13 per cent in 1949. One death occurred in the immunized group (a boy 11 years old, immunized in infancy). There was no immunization in any of the remaining 9 who died.

Course on Diagnosis of Neoplastic Disease.—The California Cancer Commission with the support of the California Division and the national office of the American Cancer Society and the Tumor Board of the Los Angeles County Hospital will present a refresher course for the practicing physician and surgeon on the diagnosis of neoplastic disease in the auditorium of the Los Angeles County General Hospital February 19-20. The following scientific papers will be presented:

R. Lee Clark Jr., Houston, Texas, Present Status of the Problem of Gastric Cancer.
Earl R. Miller, San Francisco, Roentgenographic Features of Cancer of the Gastrointestinal Tract.
Charles B. Puestow, Chicago, Cancer of the Colon, Including Rectum, Rectosigmoid and Anus.
Henry H. Searls, San Francisco, Cancer of the Breast.
Michael E. DeBakey, Houston, Texas, Cancer of the Esophagus.
Henry M. Weyrauch, San Francisco, Cancer of the Male Urinary Tract.
Howard R. Bierman, San Francisco, Malignant Lesions of the Blood and Lymph Nodes.
Robert P. Watkins, San Francisco, Malignant Bone Tumors.
Edmund W. Overstreet, San Francisco, Cancer of the Female Genital Tract.

A special tumor board will be held at the Veterans Administration Center, West Los Angeles, from 2 to 4:30 p. m. February 21, when presentation of interesting tumor cases will be made.

Awards for Essays on Tuberculosis.—The California Trudeau Society has announced its first annual award of $150 for the best paper on the clinical, laboratory or epidemiologic aspect of tuberculosis presented by a California resident. The winning paper will be presented at the society's annual meeting. The deadline for submission of papers is March 1. A sealed envelope containing the name and address of the author and title of the paper should be enclosed with the manuscript, which should not bear the name of the author. Send papers to the Trudeau Society Award Committee, 45 Second Street, Room 409, San Francisco 5.

The California Tuberculosis and Health Association will present its second annual Higby Memorial Award of $150 to a resident of California for the best paper on any sociologic, psychologic or historical aspect of tuberculosis. The deadline for submission of papers is March 1. Papers, prepared as they are for the Trudeau Society, should be sent to the Higby Memorial Award Committee, 45 Second Street, Room 409, San Francisco 5.

ILLINOIS

Communicable Diseases Decline.—An analysis of public health trends in Illinois during the last decade reveals a decided decline in the prevalence of diphtheria, scarlet fever, pneumonia, malaria, syphilis and smallpox, according to the state director of public health. Poliomyelitis, gonorrhea, undulant fever and mumps show rising rates. Those diseases which had become less prevalent in 1949 than at the beginning of the decade were whooping cough, which declined from 6,411 to 3,972 cases; tuberculosis, from 8,574 to 7,973; influenza, from 1,124 to 306; trachoma, from 323 to 14; typhoid, from 310 to 98; diphtheria, from 936 to 50; scarlet fever, from 20,814 to 4,032; measles, from 8,669 to 5,715; pneumonia, from 14,592 to 4,778; malaria, from 199 to 3; smallpox, from 167 to 0, and paratyphoid, from 19 to 2. Meningitis decreased from a peak of 996 cases in 1944 to 199 in 1949. Encephalitis, which showed a slight downward trend, varied from a high of 83 cases in 1941 to a low of 51 cases in 1942. Last year 57 cases were reported. The 13,830 cases of syphilis reported in the state last year represented a 37 per cent decline from the median of the last nine years.

Gonorrhea for the ten year period showed an increasing tendency even though a decline in the number of cases set in after 1946. Gonorrhea cases outnumber those of any other single disease. The total of venereal disease cases alone was nearly as great as that of all the other communicable diseases combined.

Chicago

Grants for Hematologic Research.—A gift of $5,000 was presented to the Michael Reese Hospital's department of hematology research by the Hematology Research Foundation in December. Organized in 1944, the foundation is composed of 1,500 Chicagoans supporting research into diseases of the blood.

McArthur Lecture.—Dr. Charles C. Macklin, head of the department of histologic research, The University of Western Ontario (Canada) Faculty of Medicine, will deliver the twenty-sixth Lewis Linn McArthur Lecture of the Frank Billings Foundation of the Institute of Medicine of Chicago on February 24 at the Palmer House on "The Alveoli of the Mammalian Lung."

Heart Association Meeting.—The Clinical Section of the Chicago Heart Association will be held February 14 from 10 a. m. to 12 noon at the Museum of Science and Industry. Papers will be given on "Presentation of 1949 Cases with Postmortem Examinations" and "Effect of Steroid Compounds (ACTH) on Rheumatic Fever." The program has been arranged by La Rabida Jackson Park Sanitarium.

Personals.—Dr. Frank C. Lawler has been appointed to the board of trustees of his alma mater, the Chicago Medical School. ——Dr. Julius B. Richmond has been promoted to the rank of professor of pediatrics at the University of Illinois College of Medicine. Last year Dr. Richmond was named a scholar in medical science by the John and Mary R. Markle Foundation of New York City. He is a member of the committee on organization of the Governor's Committee for Illinois on the Mid-Century White House Conference.

Dr. Bailey Honored.—A testimonial banquet honoring Dr. Percival Bailey was held January 23. He was presented an illuminated testimonial on behalf of the Armenian community in this area for his contribution to the cause of science and his interest in the Armenian people and their history and literature, for his helpfulness to the Armenian community and for his devotion to the Armenian cause. Dr. Bailey, professor of neurology and neurosurgery at the University of Illinois, College of Medicine, on November 26 was made an honorary doctor of the University of Paris.

IOWA

Society Lecture.—At the meeting of the Dubuque County Medical Society February 14 at the Bunker Hill Club in Dubuque, Dr. Howard M. Odell of the Mayo Clinic, Rochester, Minn., will speak on "The Nature and Management of Acute Renal Failure."

Physicians Choose Small Communities.—The Iowa State Medical Society is said to have reported that life in the small town of Iowa is proving attractive to physicians, as shown by the fact that for each doctor establishing himself in a large community of the state two doctors are setting up practice in small towns. The society said that with a few exceptions no Iowa family is more than 15 or 20 miles from a doctor at the present time. The society, however, still lists 33 towns seeking a doctor and another to help out a physician already in practice.

MICHIGAN

Annual Heart Day.—The Michigan Heart Association will meet March 11 at the Book-Cadillac Hotel, Detroit, beginning at 9 a. m., under the presidency of Dr. Warren B. Cooksey. The following program will be presented in the morning:

Irvine H. Page, Cleveland, Hypertension.
Louis N. Katz, Chicago, Arteriosclerosis.
Hugh McCulloch, Chicago, Rheumatic Fever.

Maternal Mortality Study.—On January 1 the Michigan State Medical Society's Maternal Health Committee and the Michigan Department of Health began a study of all maternal deaths in the state. The state is divided into five districts and a designated physician in each area who is a specialist certified by the American Board of Obstetrics and Gynecology or a man who is eligible for the board examinations will secure the information regarding the maternal deaths in each district within a week after the death occurs. The attending physician will be asked to notify the department of health immediately, giving the name, address and cause of death.

MINNESOTA

New Division of Mental Health.—The Division of Preventive Mental Health Services was created by the state board of health at its meeting December 16. The new division supersedes the old Mental Health Unit, created by the Board of Health in December 1947, when the department initiated the state's preventive mental hygiene program made possible by federal funds received under the Mental Health Act of 1946. Mr. William Griffiths, who has been acting supervisor of the Mental Health Unit, is now acting director of the new division, with Dr. Reynold A. Jensen, associate professor of pediatrics and psychiatry at the University of Minnesota, as consultant. Full time staff members include a public health nurse and a health educator with training in psychology.

NEW YORK

University Appointment.—Dr. Robert W. Graves, Rome, Ga., has been appointed professor of neurology at Albany Medical College and attending neurologist at Albany Hospital. He is a graduate of Duke University School of Medicine, Durham, N. C. (1933), and did postgraduate studies in neurology at the Montreal (Canada) Neurological Institute, the National Hospital in London and the Institute of Cancer in Madrid.

Special Care for Premature Infants.—A program of special care for premature infants was begun January 1 by the New York State Department of Health. At present it will center around Buffalo Children's Hospital and will cover six western counties that make up the Buffalo State Health Region. In time it is hoped to extend the program to the remaining four up-state health regions. An annual appropriation of $35,000 has been made available. Transportation from the place of birth to the hospital will be by special ambulance. Parents will be expected to pay as much as they could reasonably afford toward the cost of the special care.

New Unit for Receiving Rheumatic Fever Cases.—Irvington House, Irvington, has opened a new unit to receive children with acute rheumatic fever. Children of either sex between the ages of 6 and 14 will be eligible for admission, and preference will be given to those who are seen very early in the attack and in whom no therapy has been started. Before the establishment of the new unit Irvington House operated as a school-sanatorium with patients referred from hospitals of Greater New York and Westchester County. The hospital unit will change this procedure by accepting patients directly from the doctor. Dr. Harold C. Anderson, formerly of the Rockefeller Institute for Medical Research, is in charge of research and medical activities. During the past 29 years more than 3,200 underprivileged children have received free rehabilitative care at Irvington House.

New York City

Clearing House for Aid to the Handicapped.—New York University College of Medicine will establish a reference center for listing up-to-date information on aids and assistive appliances for the rehabilitation of handicapped persons. This material, assembled under the direction of Dr. Howard A. Rusk, chairman, department of physical medicine and rehabilitation, will be assembled in loose-leaf manual form for distribution to hospitals, agencies and certain professional individuals. Models of such equipment will be maintained at the center for teaching purposes and further development. The center will be established through a March of Dimes grant of $19,332.

Graduate Course in Compensation Medicine.—This course will be given by the New York University Post-Graduate Medical School and the American Academy of Compensation Medicine February 27 to March 4 in Erdmann Auditorium of University Hospital. Subjects of succeeding half-day sessions are dermatology; pathology; diagnosis and treatment of arthritis in relation to compensation medicine; peripheral vascular disease with case presentation; pulmonary diseases; orthopedic problems in compensation medicine; occupational diseases; neurology, neurosurgery and psychiatry; rehabilitation; tumors, and radiology, which will be given a full day's discussion. The tuition fee is $25. For information address Office of the Dean, New York University Post-Graduate Medical School, 477 First Avenue, New York 16.

Report on Municipal Hospitals.—In his annual report, Dr. Marcus D. Kogel, commissioner of hospitals, January 5 declared that, despite the greatest patient load ever cared for by the municipal hospitals, they were not forced to turn away a single patient requiring emergency care in 1949, principally because of the Home Care program launched last year. Harlem Hospital maintained its position as the most crowded hospital in the department, with a percentage occupancy of 140.5. Greenpoint Hospital in Brooklyn holds the record for the lowest percentage occupancy, 82.1. Commissioner Kogel said that the percentage of occupancy averaged 100.9 for last year, compared with 99.2 in 1948, and that it would have been impossible to provide hospitalization for the indigent sick without Home Care, which accounts for 186,000 days of care for 2,500 patients, who received 12,000 home visits by physicians, 28,000 visits by nurses, 3,500 by medical social workers, 5,400 by physical therapists, 200 plus by occupational therapists and about 57,000 hours of housekeeping service. The operation of Home Care indicates a per capita per diem cost of $2.66, or about one-fourth the current daily cost for general care in the municipal hospital wards. A significant advance during 1949 was the reorganization and expansion of the anesthesia services. Specialists in the field have been invited to head these departments, and in some cases a fee for service basis has been established in order to insure a continuing high quality of professional skill in institutions which, because of lack of medical school affiliations or other reasons, have found difficulty in recruiting anesthesiologists of high caliber.

SOUTH DAKOTA

Open Tumor Treatment Clinic.—A group of Yankton physicians on the staff of Sacred Heart Hospital and faculty members of the University of South Dakota School of Medical Sciences, Vermillion, organized the state's first tumor treatment clinic at the hospital, where on Tuesday and Friday mornings patients are brought in by their doctors for consultation concerning treatment. The South Dakota Division of the American Cancer Society contributes to the financial support of the clinic, has supplied the files and record system and helps pay for the part time secretary. The clinic is not a cancer detection center; it does not attempt to give a diagnosis for any patient whose doctor is not certain that a tumor exists. At the clinic the patient is examined, roentgenograms and laboratory findings are studied and from this treatment is recommended. The clinic is set up according to the standard system prescribed by the American College of Surgeons and the American Cancer Society. Any doctor may bring a patient to the clinic for this consultation, which is free. Sacred Heart Hospital has to charge for the use of its equipment if the patient takes treatments there, but the recommended treatment can be taken wherever the patient and his doctor choose. Tumor specimens, which formerly had to be sent out of the state for examination, can now be examined at this clinic.

TEXAS

Alpha Pi Alpha Lecture.—This annual lecture will be given February 16 at 8 p.m. at the Baylor University Hospital Auditorium by Dr. Michael E. DeBakey, professor of surgery at Baylor, Houston, on "Arteriosclerotic Peripheral Vascular Disease."

Neurologic Clinics for Children.—Dr. Douglas N. Buchanan of the University of Chicago will be visiting lecturer under the auspices of the Child Health Program of the University of Texas, Medical Branch, Galveston, March 6-18. Dr. Arild E. Hansen, director of the Child Health Program, has arranged for a series of special neurologic clinics for children at the Children's Hospital. Physicians are cordially invited to attend.

Internists Society.—The Texas Academy of Internal Medicine was formed in December at a meeting in Dallas, with Dr. Samuel A. Shelburne of Dallas as president. Dr. John S. Chapman, Dallas, was elected secretary-treasurer for three years. The academy has 175 members. Physicians eligible for membership must be certified by the American Board of Internal Medicine or must be fellows for the American College of Physicians. Annual meetings will rotate through the three cities where medical schools are located, Dallas, Houston and Galveston.

WEST VIRGINIA

Conference on Public Health.—The School of Medicine, West Virginia University, is sponsoring a two day meeting March 31 and April 1 on public health to meet the interest of all persons working in public health and those interested in the promotion of public health. Surgeon General Leonard A. Scheele, Washington, D. C., will be the banquet speaker. Out of state speakers who are leaders in their respective fields will discuss sanitation, epidemiology, mental health, tuberculosis, nursing and industrial hygiene; sufficient time will be allowed for discussion periods.

Registration of Licensed Physicians.—A total of 1,649 West Virginia doctors have renewed their licenses to practice medicine in West Virginia under the reregistration law which became effective July 1, 1949. In addition, 198 doctors residing outside West Virginia have renewed their licenses for the biennium. The registration, which has been completed by the state department of health, also includes the names of 54 West Virginia doctors who have retired from practice. This would indicate that there are 1,595 doctors in active practice in the state at present. A report submitted on January 8 to the council of the West Virginia State Medical Association disclosed the fact that the membership of the association has reached an all-time high of 1,425. Of this number 125 doctors are honorary members.

PUERTO RICO

Rehabilitation Problems.—The first Institute on Rehabilitation Problems in Puerto Rico was held at the School of Tropical Medicine in San Juan February 1-4. Dr. Donald A. Covalt, associate professor of physical medicine and rehabilitation, and Eugene J. Taylor, instructor in physical medicine and rehabilitation, both members of the faculty of New York University College of Medicine, were among the speakers. The purpose of the conference was to make recommendations for the development of adequate rehabilitation facilities.

GENERAL

Pan-American Doctors' Club.—This club's semiannual medical meetings will be held at Hacienda San Miguel Regla, Hidalgo, Mexico, from February 28 to March 1. The meetings are open equally to members and nonmembers. Arrangements for attendance should be made with Dr. C. A. Mills, Secretary, Cincinnati General Hospital, Cincinnati 29.

Conference on Industrial Medicine.—The New England Conference of Industrial Physicians and Surgeons will meet February 15 at 183 Middlesex Ave., Somerville, Mass., with the Ford Motor Company as host. Dr. Dwight E. Harken, assistant professor of surgery, Tufts College Medical School, Boston, will present colored motion pictures on heart surgery at 2 p. m.

Booklet on Medical Diagnostic Services.—The W. K. Kellogg Foundation, Battle Creek, Mich., has published a booklet entitled Medical Diagnostic Services for Small Communities. Thirty-nine pages and appendixes point out the need for good medical diagnostic services, where they should be placed, technicians, equipment and costs needed and a model plan for community units.

Dr. de Forest Appointed Medical Director.—Dr. Gideon K. de Forest of New Haven, Conn., has been appointed medical director of the Arthritis and Rheumatism Foundation. Dr. de Forest is assistant clinical professor of medicine at Yale University and assistant attending physician at Grace New Haven Hospital.

Hebrew Medical Journal.—This bilingual semiannual journal concluded its twenty-second year of publication with the appearance of volume 2, 1949, in which issue, among numerous others, is an article by Prof. A. S. Yahuda on "Medical and Anatomical Terms in the Pentateuch in the Light of Egyptian Medical Papyri" and another by Zussmann Munter, M.D., on "Jews as Intermediaries of Medicine and Natural Science During the Middle Ages." The editor of this journal is Dr. Moses Einhorn, and the editorial office is at 983 Park Avenue, New York 28.

Medical Missions Program.—The Unitarian Service Committee, New York, lists the following results of its medical mission program: The University of Vienna has introduced interdepartmental conferences, established anesthesiology as a medical specialty in the university and has developed plans for an Austrian Research Council. Poland has begun to give some special instruction in anesthesiology. Over 1,000 new medical texthooks were placed in medical libraries of medical schools visited by various missions, and a large number of journals and older texthooks have also been sent to the libraries. After the mission to the Philippines, not only was $100,000 made available to implement a BCG program but personnel was sent to Denmark for specialized study in this field. Medical missions will continue in 1950, when three or four missions will be sent to countries in Europe, the Middle East, the Orient and Latin America, which have indicated directly or indirectly that they would welcome service committee missions.

Occupational Medicine Meeting.—The second annual meeting of the American Academy of Occupational Medicine will be held at the Netherlands Plaza Hotel, Cincinnati, February 17-18, under the presidency of Dr. Robert A. Kehoe, Cincinnati. The following papers, to be followed by discussion, will be presented the first day:

Irving R. Tabershaw, New York, Relationship of Health Insurance to the Practice of Industrial Medicine.
Milton H. Kronenberg, Peoria, Ill., Report on Resident Training for the Industrial Physician.
Frank Princi, Denver, Cadmium Poisoning.
James H. Sterner, Rochester, N. Y., Some of the Medical Aspects of Atomic Energy.

At the evening session following the dinner Friday night Dr. Stanley E. Dorst, dean of the University of Cincinnati College of Medicine, will make an informal report on certain aspects of the medical situation in Great Britain. The second day will feature a tour of the Kettering Laboratory of the University of Cincinnati College of Medicine to observe and discuss experimental work in progress.

Births, Deaths and Marriages in 1949.—About 3,700,000 babies were born in the United States in 1949, according to the statisticians of the Metropolitan Life Insurance Company. It was the third year in succession in which the number of births exceeded 3,500,000. The general health record of the country was also extraordinarily good in 1949. Present indications are that the death rate for the year was about 9.7 per 1,000, or about 2 per cent under the previous minimum set in 1948. The high birth rate, combined with the lowest death rate on record and a sizable immigration, increased the population of the U. S. by 2,500,000 during the year. This brought the total population figure to about 150,500,000 at the end of 1949. The infant mortality rate declined during 1949 to a new minimum of 31 per 1,000 live births. The steady decline in infant mortality during the decade has meant an aggregate saving of nearly 325,000 lives among babies born during this period.

About 1,580,000 couples married in the United States in 1949, a decline of one eighth from 1948 and nearly one third less than the all-time peak of 2,291,000 marriages in 1946. Despite recent declines, the yearly number of marriages is still above the prewar level.

Handbook on Study Abroad.—A total of 21,751 opportunities for foreign study, observation and research are reported in a new edition of the United Nations Educational, Scientific and Cultural Organization handbook, "Study Abroad." The list of fellowships, scholarships and grants-in-aid, classified according to the country of origin, credits the United States with 5,096 awards made through private and governmental sources. Fifty-two other nations and 23 territories also are represented. The current study contains a survey of the teacher exchange program participated in by 3,000 teachers in 18 countries and relates the growth in exchanges whereby workers

have visited other lands for vocational purposes. In another section, "Study Abroad" describes the work of 180 national and international organizations sponsoring educational exchanges of young people. As the only single source of detailed information gathered on a worldwide scale, the handbook serves as a directory for those seeking study opportunities. Nearly half the awards catalogued by UNESCO are in unspecified fields, thus allowing most candidates a wide choice of study. In the special categories are 1,148 awards in medical sciences. Copies of "Study Abroad" may be obtained from the Columbia University Press, 2960 Broadway, New York, at $1.25 each.

Establish Waksman Foundation in France.—The Trustees of Rutgers University Research and Endowment Foundation, holder of patents on streptomycin and other antibiotics developed by Dr. Selman A. Waksman, department of microbiology of Rutgers University, have approved the establishment of a foundation to encourage microbiologic investigations in France, which is to be known as the Waksman Foundation. This foundation was launched with an initial contribution of 3,000,000 francs from Rhone-Poulenc, French chemical concern, which has been licensed by the Rutgers Research and Endowment Foundation to engage in the manufacture of streptomycin in France, and it will pay the royalties due to the Rutgers Foundation to the new French foundation. The funds will be used for the support in France of research on antibiotics and on other problems in the field of microbiology. Four grants, totaling 2,140,000 francs, were proposed by the committee of the French foundation at its first meeting in December. Three of the grants will go to workers at the Pasteur Institute in collaboration with various hospitals in Paris, and the other to a staff member in the biochemical laboratories of the Ministry of the Colonies. The executive committee of the French foundation consists of a representative of the French Academy of Medicine; Prof. Jacques Trefouel, member of the French Institute and director of the Pasteur Institute, and Prof. R. Paul, scientific director of Rhone-Poulenc.

Veterinary Public Health Section Created.—To promote national programs in the veterinary aspects of public health and to coordinate the international phases of such programs, the Pan American Sanitary Bureau (Regional Office of the World Health Organization) has created a Veterinary Public Health Section. The list of diseases known to be transmissible from animals to man is long. Important diseases not often considered in the light of their veterinary public health importance include jungle yellow fever, sylvatic plague, schistosomiasis, leptospirosis, Rocky Mountain spotted fever and various encephalitides. One of the first steps taken by the new section is the inauguration of an international campaign of rabies control along the United States-Mexican border. Recently Mexican scientists, under the auspices of the bureau, visited U. S. Public Health Service establishments and laid the basis for international team work in the control of the disease along the border. The bureau will soon engage in an active campaign in the Rio de la Plata area against hyatidosis. Although this disease threatens mainly Uruguay, Argentina, Paraguay and the southern part of Brazil, it is said to be gradually extending to adjacent areas. The bureau will promote an active public education project concerning this disease, along with a program for controlling the disease in the animal reservoir. Special studies of brucellosis are now in progress, and the Third Inter-American Brucellosis Congress is scheduled for meeting in Washington, D. C., in November, jointly sponsored by the Brucellosis Committee of the U. S. National Research Council and the sanitary bureau.

The newly created division of the bureau will act as an intercontinental clearing house for information in the relations between animal and human health. Chief of the new section is Benjamin D. Blood, who pioneered in the development of the Air Force Veterinary Service.

FOREIGN

Congress on Gastroenterology.—The Second European Congress of the Spanish Association of Gastroenterology will meet in Madrid May 4-7. The general theme will be diseases of the biliary tract, except lithiasis and cancer. Those presenting papers include: Professor Gregory, Liverpool; Dr. Revers, Utrecht; Jimenez Diaz, Madrid; Professor Chiray and Dr. Caroli, Paris; Dr. Pavel, Bucharest; Professor Mallet-Guy, Lyon; Professor Odin Goteborg and Dr. Lagerlof, Stockholm; Professor Kapp, Basilea; Dr. Gallart Mones, Barcelona; Professor Santos, Lisbon; Professor Nicod, Lausanne; Professor Hernando, Madrid; Dr. Douthwaithe, London; Professor Herlstrom, Stockholm; Dr. Massion, Bruxelles; Professors Van Goidsenhoven and Applemans, Louvain, and Professor Casbarrini, Bologna. As guests, Professor Mirizzi, Cordoba, and Drs. Bengolea and Velasco Suarez, Buenos Aires, will discuss surgical cholangiography and duodenal catheterism, respectively. Those who expect to attend are requested to send in their application to the General Secretary, Jorge Juan 41, Madrid, not later than March 1. All members will have the right to take part in the discussion and present papers on the general theme. One session will be devoted to the reading of papers dealing with selected subjects. These must not exceed 600 words.

Medicolegal Days.—The Italian Congress of Legal and Insurance Medicine has designated Viareggio as the seat of "Medicolegal Days," to be held in the second half of May 1950. The subjects of reports to be presented are as follows: Recent Progress: (1) in research on blood, T. Formaggio, Pavia; (2) in blood transfusion, A. Fornari, Pisa, and (3) in blood tests, F. Tarstino, Naples. The reports will be printed in a special issue of *Minerva Medica* and will be sent one month ahead of the meetings to all those who plan to attend the convention. Titles of papers to be presented should be sent to the Office of the Secretary of the Convention, Istituto di Medicina Legale e delle Assicarazioni, Via Roma, 33, Pisa, Italy, not later than March 31. Notification of attendance should be accompanied with a postal money order or check in the amount of 1,000 lire ($1.30) payable to Dr. A. E. Vitolo, secretary of the convention.

Argentina Fellowships for Foreigners.—The Ministry of Public Health, Republic of Argentina, is offering 20 annual scholarships of 1,000 pesos for professional foreigners to study sanitation in Argentina. Scholarships are for one year but can be renewed if results of the work justify it. Candidates must present a documented list of their professional and scientific background and a detailed plan of the studies they wish to make and specify the date they wish to begin studying and the institution they prefer to attend. A sufficient knowledge of Spanish is necessary. The Scholarship Section of the ministry will take care of the travel of those granted scholarships and will send them to the study center, which may or may not be subsidiaries of the Ministry of Public Health. The selection of the candidates will be made according to their personal qualifications and to the importance of the work they have to perform in their own countries. Applications will be made only through the sanitary authorities of the universities of the native country, who will agree officially to offer to the recipient of the scholarship, on his return, a job that he will accept and afterward apply the knowledge he has acquired. Those interested can secure an application blank from the Educational Programs Branch, Division of International Health, U. S. Public Health Service, Washington, D. C.

CORRECTION

New Diagnostic Adjunct for Uterine Cancer.—In the article by Odell and Burt in THE JOURNAL, January 28, page 227, right hand column, line seven, the phrase "with 30 units used" should read "with 300 units used."

Conteben.—In the editorial on page 343 in THE JOURNAL, February 4, the thirteenth line from the bottom of the first column, which reads "These authors feel that conteben antituberculous activity of the same general order as that . . ." should read "These authors feel that conteben antituberculous activity appears to be of the same general order as that . . . ."

Marriages

ROBERT CORLETT HOWARD, Chicago, to Miss Frances Enderlin Booth at Larchmont, N. Y., December 17.

GARRY DE NEUVILLE HOUGH III, Longmeadow, Mass., to Miss Nancy Ann Greer at Belmont, January 7.

REX MITCHELL BLEAKNEY, Columbus, Ohio, to Miss Helen E. Ritter in Louisville, Ky., November 2.

WILLIAM ROSEN to Miss Mary Louise Sullivan, both of New Bedford, Mass., December 26.

JOHN CHRISTIAN RANSMEIER to Miss Frances Ellen Starnes, both of Atlanta, Ga., December 31.

LINCOLN D. CLARK, Andover, Mass., to DR. EDITH LOUISE STONE of South Lincoln, recently.

JAMES ENNIS SHEEHAN to Miss Patricia D. Gallagher, both of Brooklyn, December 31.

WILLIAM PATRICK LONG, Los Angeles, to Miss June O'Connor of Chicago, November 26.

Deaths

Lee Connel Gatewood ● Chicago; born in Stockport, Ohio, March 15, 1889; Rush Medical College, Chicago, 1911; clinical professor of medicine at the University of Illinois College of Medicine; specialist certified by the American Board of Internal Medicine; member of the Central Society for Clinical Research and American Gastro-Enterological Association; fellow of the American College of Physicians; served during World War I and received a citation for "meritorious and conspicuous service"; affiliated with Delnor Hospital in St. Charles, Lake Forest (Ill.) Hospital, Highland Park (Ill.) Hospital and Presbyterian Hospital, Chicago; died January 3, aged 60, of coronary thrombosis.

Leonard Harriman ● Howard Lake, Minn.; College of Physicians and Surgeons of Chicago, School of Medicine of the University, 1909; veteran of the Spanish-American War; for many years president of the school board, health officer and president of the Security State Bank; died in Cokato (Minn.) Hospital November 25, aged 76, of uremia.

Carl Francis Hollenback ● Omaha; University of Nebraska College of Medicine, Omaha, 1918; died December 20, aged 58, of heart disease.

George Hunter, Blairsville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1886; director of the Blairsville National Bank; died December 19, aged 86, of cerebral hemorrhage.

Alfred Norman Jennings, San Bernardino, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1935; certified by the National Board of Medical Examiners; member of the American Medical Association; medical examiner for the draft board during World War II; formerly local surgeon for the Santa Fe Railroad; died November 30, aged 46, of hypertensive heart disease.

Edward Charles Koenig ● Buffalo; University of Buffalo School of Medicine, 1904; formerly on the faculty of his alma mater; specialist certified by the American Board of Radiology; fellow of the American College of Physicians; member of the American Roentgen Ray Society, Radiological Society of North America and the American College of Radiology; served overseas during World War I; on the staff of the Buffalo General Hospital, where he died December 19, aged 72, of acute coronary occlusion.

Wilfred Streng Ley ● Hawthorne, Calif.; Wayne University College of Medicine, Detroit, 1942; member of the Michigan State Medical Society; served during World War II; died December 19, aged 36.

Louis Joseph Lista, San Francisco; Regia Università degli Studi di Siena Facolta di Medicina e Chirurgia, Italy, 1928; served during World War I; formerly health officer of Siskiyou County; died December 6, aged 53, of leukemia.

Courtney S. McGuire, Maysville, Ky.; Kentucky School of Medicine, Louisville, 1906; member of the American Medical Association; died December 16, aged 72, of coronary sclerosis.

Harry Ahrend Meyer, Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1905; member of the American Medical Association; affiliated with Manhattan General Hospital, New York; died in Beth Israel Hospital January 2, aged 67, of a cerebrovascular accident and arteriosclerosis.

John James Morrow ● Mountain Home, Ark.; University of Arkansas School of Medicine, Little Rock, 1889; past president of the Ninth Councilor District Medical Society; at one time mayor of Cotter; died December 14, aged 88, of virus pneumonia and chronic nephritis.

Edward Ralph Myers, Pittston, Pa.; Jefferson Medical College of Philadelphia, 1903; died December 5, aged 71, of adenocarcinoma of the rectum.

Israel Jay Rachlin, South Orange, N. J.; University and Bellevue Hospital Medical College, New York, 1903; for many years affiliated with the Beth Israel Hospital in Newark; president of the Union Building Company and Albert M. Greenfield & Company in Newark; died December 5, aged 68, of amyotrophic lateral sclerosis.

Alexander Nicholas Talley Roach, Mobile, Ala.; University of the South Medical Department, Sewanee, Tenn., 1901; member of the American Medical Association; died December 15, aged 71, of carcinoma of the larynx.

Durward Belmont Roach, Hopkinsville, Ky.; Kentucky School of Medicine, Louisville, 1906; member of the American Medical Association; died November 22, aged 66, of cerebral hemorrhage.

Thomas J. Robinson, Wilmar, Ark. (licensed in Arkansas in 1903); died in Little Rock November 29, aged 75, of pneumonia.

Samuel Rosenfeld Jr. ● Columbus, Ohio; Rush Medical College, Chicago, 1936; on the faculty of the Ohio State University College of Medicine; died December 7, aged 42, of acute coronary infarction.

Allen Robert Rozar ● Macon, Ga.; Atlanta School of Medicine, 1911; member of the Southeastern Surgical Congress; formerly member of the state board of health; fellow of the American College of Surgeons; served as secretary-treasurer and later as president of the Bibb County Medical Society; formerly vice president of the Medical Association of Georgia; for many years on the staff of the Macon and Mercy hospitals; died December 11, aged 61, of coronary thrombosis.

Ella M. Russell, Chambersburg, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1906; formerly on the faculty of her alma mater; served on the staff of the Chambersburg Hospital, where she died December 5, aged 71, following an operation for carcinoma of the uterus.

Ira M. Sanders ● Greensburg, Ind.; Medical College of Indiana, Indianapolis, 1896; director of the Decatur County National Bank; died December 10, aged 78, of coronary thrombosis.

Ernst P. E. Sengstak, Daytona Beach, Fla.; Baylor University College of Medicine, Dallas, 1905; member of the American Medical Association; died December 5, aged 72, of virus pneumonia.

Rufus George Shanks, Autaugaville, Ala.; Memphis (Tenn.) Hospital Medical College, 1901; member of the American Medical Association; died October 11, aged 74, of coronary occlusion.

Franklin Clarence Spalding, West Point, Miss.; Memphis (Tenn.) Hospital Medical College, 1901; member of the American Medical Association; died December 16, aged 72, of heart disease.

Ernest Stengel ● New York; Medizinische Fakultät der Universität, Wien, Austria, 1924; associated with the Hospital for Joint Diseases; died in December, aged 51.

David Charles Throop, Rochester, N. Y.; Trinity Medical College, Toronto, Ontario, Canada, 1885; died December 10, aged 89, of myocarditis and arteriosclerosis.

Reece C. Townsend, Milwaukee; Medical College of Ohio, Cincinnati, 1890; died in Milwaukee County Hospital November 6, aged 82, of chronic myelogenous leukemia.

Charles R. Unkrich, Whitewater, Wis.; Hering Medical College, Chicago, 1899; died in the Lakeland Hospital, Elkhorn, November 29, aged 75, of uremia, fracture of the left hip due to a fall and arteriosclerosis.

Frank Bunnell Voght, Buffalo; Niagara University Medical Department, Buffalo, 1889; died in Deaconess Hospital December 12, aged 83, of uremia and enlarged prostate.

Oran Douglas Ward, England, Ark.; University of Nashville (Tenn.) Medical Department, 1902; member of the American Medical Association; past president of the Lonoke County Medical Society, of which he had been secretary and treasurer; served as member of the State Medical Board of the Arkansas Medical Society; died in Little Rock December 12, aged 74, of arteriosclerotic heart disease.

Llewellyn G. Wedgwood, Grandville, Mich.; Detroit College of Medicine, 1899; member of the American Medical Association; for many years health officer and member of the school board; died in St. Mary's Hospital, Grand Rapids, December 5, aged 76, of right bundle branch block and coronary insufficiency.

August William Werner, Quincy, Ill.; Bennett Medical College, Chicago, 1898; member of the American Medical Association; for many years on the staff of Blessing Hospital; died in St. Mary's Hospital December 24, aged 78, of acute miliary tuberculosis.

Raymond Francis Wivell, Pittsburgh; University of Pennsylvania School of Medicine, Philadelphia, 1917; served during World War I and for local draft board during World War II; school physician for department of child welfare; formerly on the staff of St. John's Hospital; died in Mercy Hospital recently, aged 56, of carcinoma of the liver.

● Indicates Fellow of the American Medical Association.

Foreign Letters

PARIS

(From a Regular Correspondent)

Nov. 15, 1949.

Treatment of Congenital Heart Disease

In January 1948, the "Centre of Blue Children" was created at the Broussais Hospital. It first was intended for the surgical treatment of Fallot's tetrad but has since been extended to permit intervention in other congenital or acquired cardiopathies. One hundred and forty children suffering from Fallot's tetrad have been subjected to the operation, of which Professor d'Allaines, Donzelot and their co-workers report the first results. They always try to effect anastomosis between one of the branches of the aorta and the corresponding pulmonary artery; they have obtained excellent results with Pott's laterolateral anastomosis. Of 140 cases they have noted 15 per cent deaths, 10 per cent operative failures and 75 per cent favorable results. In one group, physical activity was considerably improved, but cyanosis either remained permanently or occurred in the presence of tiredness or anger. In another group, improvement was much more noticeable because of the children's complete transformation. A last group of subjects, almost crippled before the operation, have become capable of activities such as riding on a bicycle. None of the 105 surgically treated patients who were cured died within the last eighteen months. Some have developed other severe diseases and have withstood them.

Other congenital cardiopathies, such as the stenosis of the aortic isthmus, and pulmonary stenosis other than Fallot's have been operated on with the same success. In 3 of 16 subjects with an isolated persistency of the arterial channel (5 for more than 20 years and 11 for 8 to 18 years) explorative interventions and 13 ligatures were performed. The murmur has disappeared, and functional disorders have been improved.

In acquired cardiopathies, the authors have applied the ligature of the vena cava to patients with an intractable mitral deficiency, as well as to patients with left ventricular deficiencies of various types. Of 11 patients operated on, 2 moribund patients with asystolic conditions died and 9 were considerably improved with respect to their pulmonary and cardiac condition. Within 2 weeks radiography showed a diminution of the heart and a normal transparency of the lungs. At the meeting of the National Academy of Medicine on July 5, 1949, at which the authors presented these results, Professor Laubry stressed the importance of this communication. He pointed out that in cardiac deficiencies the role of the nervous system in purely mechanical disorders should not be ignored.

Gastroduodenal Ulcers

R. Carvaillo, who has studied ulcers for ten years, believes their sudden onset and determination are due to tissue modifications that are somewhat similar to those observed in immunity, which disappear after a time and would thus account for the evolutive cycle of the disease. He has used serum from a patient with ulcers who has experienced long periods of remission, on other patients suffering from the same disease but not responding to the usual treatments.

He observed interesting results, but to prove that this effect was not due to psychologic factors he used injections of normal or antidiphtheric serum, which did not produce similar results. Professor Marcenac and Dr. Bordet, of the National Veterinary School of Alfort, have stated that this type of serum protects the rat against experimental ulcer, whereas serum from a nonulcerous donor is ineffective. With the cooperation of Dr. Gutman, a center for the collection of serum from ulcerous patients has been created at the St. Antoine Hospital, to permit a larger experiment with this method of treatment. In the last issue of the *Le Monde Médical*, Carvaillo published the results in 300 cases.

Death of Professor Fourneau

E. Fourneau, a chemist of universal reputation and a member of the National Academy of Medicine, died at the age of 77. He was one of the pioneers of chemotherapy in France. Fourneau had directed the activities of the Laboratory of Chemotherapy of the Pasteur Institute since its creation in 1911. Almost no field remained foreign to his activity. He discovered stovaine (amylocaine hydrochloride), and studied the pentavalent arsenicals, which led to the discovery of acetarsone, effective on the spirochetes of syphilis, certain intestinal parasites and Plasmodium malariae, and its isomer 270 F., orsanine (sodium salt of an isomer of acetarsone), effective on various Trypanosoma. His work on the 10 isomer oxyphenylarsinic acids has permitted the establishment of fundamental laws. Fourneau made researches on mercury derivatives, synthetic antipaludeals, cobra venom and lysolecithin. By his works, undertaken with F. Nitti and D. Bovet, he revealed the roles of sulfonamides and sulfones in the fight against microbes. Other researches, in collaboration with D. Bovet, concerned the first synthetic sympatheticolytics, antihistaminics and spasmolytics. He also contributed to studies on hypnotics, alkaloids (yohimbine, ephedrine), amino-alcohols and curare. Fourneau was a great leader and leaves numerous French and foreign disciples. At the meeting of the National Academy of Medicine, Oct. 8, 1949, J. Trefouel, director of the Pasteur Institute, delivered a speech in commemoration of his late master.

SWEDEN

(From a Regular Correspondent)

STOCKHOLM, Jan. 13, 1950.

Poliomyelitis Research

On the recommendations of the Swedish Medical Research Council, the state has granted awards for a wide field of medical research. Isotopes are prominent, as is research on the mechanism of virus reproduction. Financial support was also provided for the investigation of disturbances of the circulation with special reference to pregnancy, hypertonia and cardiac insufficiency. An award of 79,452 kronor was granted to Prof. Sven Gard for further research into the epidemiology of acute poliomyelitis. Professor Gard's plan reflects the belief that poliomyelitis is in most instances "silent," the virus and host adapting themselves to each other without clinical manifestations of disease. In Professor Gard's opinion, epidemiologic research should be directed toward increasing our knowledge of the incidence of such infections and investigating the etiologic continuity of the so-called epidemics. He proposes to carry out for a year continuous control of the incidence of the virus in the sewage of Stockholm. Search for the virus also will be made in epidemic areas, in limited sections of which everyone will be examined systematically. These epidemic areas are to be representative of both thinly populated and densely populated districts. The various strains isolated are to be tested with reference to their effect on laboratory animals. Immunologic type determinations at present cannot be made in Sweden, and the cooperation of two American laboratories has been secured in this particular field. However, the serologic identification of certain strains pathogenic for mice can be made in Sweden.

Professor Gard also proposes to carry out systematic blood tests of patients treated in a hospital for poliomyelitis. Histologic investigations will be made of material derived from human beings and experimental animals with special reference to the "hitherto neglected muscle pathology" and to the central and peripheral nervous system. The Theiler virus and the Teschen virus will be the subject of further investigations.

The Falling and Shifting Tuberculosis Death Rate

Statistics on tuberculosis published late in 1949 by the Swedish Antituberculosis National Association reveal some curious and to a certain extent hopeful trends in the behavior of tuberculosis at the present time. Not long ago the age group in which tuberculosis developed most frequently was 20 to 24 years. Now the peak for the tuberculosis death rate has shifted to a higher age, especially for men. The notifications of deaths due to tuberculosis (all forms) in 1948 were in the ratio of 0.41 per 1,000 inhabitants, whereas in 1946 and 1947 it was 0.51 per 1,000. However, even with this reduction in the tuberculosis death rate, there are only three other causes of death claiming more victims—diseases of the heart and blood vessels, diseases of old age and cancer.

The association has organized a network of tuberculosis dispensaries on which a campaign against this disease hinges. The cooperation of these dispensaries with various hospitals, nursing homes and sanatoriums provides effective and selective treatment for the special needs of each case. Illustrative of the efficiency of the information service of the central dispensaries is the fact that about 86 per cent of the deaths from tuberculosis registered in 1948 concerned patients already on the registers of these dispensaries. Their statistics show that between the ages of 20 and 30 the tuberculosis death rate used to be higher for women than for men. In the period 1936-1940 the tuberculosis death rate was almost as high between the ages of 60 and 70 as it was between the ages of 20 and 30. In the period 1941-1945, this shift of the tuberculosis death rate to higher ages was still more marked, and for the first time this five year period showed a higher tuberculosis death rate for men than for women. This sex difference was also noticeable between the ages of 20 and 30. Before 1936 the tuberculosis death rate was higher for women than for men, but since then it has been consistently higher for men. This sex difference is particularly outstanding after the age of 35. After the age of 55 there is a rise in the tuberculosis death rate for men.

Tests for Alcohol in the Blood of Motorists

"Pro mille" is a term which haunts every motorists who is not a total abstainer, as it conjures up visions of imprisonment, fines and loss of one's driving license. According to the regulations which date from 1941 and which are still in force, a concentration of 1.5 parts per thousand or more of alcohol in the blood may precipitate a maximum sentence of one year in prison. When the concentration of alcohol in the blood is as high as 0.8, but not as high as 1.5, per thousand, the maximum sentence is six months in prison. According to some debates in the Swedish Parliament during 1949, some Swedes consider that the legislation now in force is not strict enough. It was argued that the limit of 0.8 per thousand is too lenient and that even a limit of 0.3 per thousand should not be permitted. The debaters asked whether it would not be wiser to teach the public that even minute doses of alcohol may impair a driver's judgment and reflexes and whether it would not be well to forbid the consumption of any alcohol for a certain time before driving as well as when driving. Voices were also raised in parliament in favor of more deterrent sentences on "pro mille" drivers. These debates did not lead to any new legislation, but they did serve a useful purpose in permitting the airing of grievances.

Shortage of Psychiatrists

In the first number of the *Journal of the Swedish Medical Association* for 1950, Dr. Bengt J. Lindberg from Gothenburg deplores the recent proposal that the present shortage of skilled psychiatrists in Sweden should be alleviated by the importation of a great number of psychiatrists from Austria. How, he asks, are these Austrians to wrestle satisfactorily with the Swedish language, for "speech is and remains the most sensitive and important instrument in the hands of the psychiatrist." Speech being of less importance in the other disciplines, would it not be well, he suggests, for them to receive a new infusion of Austrian blood so that more Swedish doctors would be set free to master psychiatry?

ITALY

(From a Regular Correspondent)

FLORENCE, Dec. 5, 1949.

Cavity Aspiration, Cauterization and Irradiation Treatment

Intracavitary aspiration, cavity cauterization and irradiation treatment were discussed extensively during "Medical Days" in Verona, to which reference has been made in previous letters. Professor Monaldi, director of the Istituto Sanatoriale di Napoli, presented a report on intracavitary aspiration in the management of pulmonary tuberculosis. He stated that this important subject presented two essential problems: evaluation of the therapeutic range of the method and definition of its role in the cure of specific pulmonary lesions.

In the first application of the method, the immediate, local and general results became manifest so rapidly and proved so important that they cannot be compared with results of any other type of physiomechanical procedure. Nevertheless, there are great difficulties during the terminal period of treatment, and the treated cavities may reopen. The speaker concluded that intracavitary aspiration becomes the treatment of choice in preparation for or in association with a large number of thoracoplasties and an integrating or complementary intervention in thoracoplasty with an incomplete result. In a short time this therapeutic rule has come to be followed in various countries, but, according to the speaker, the most important aspect of the problem, consideration of aspiration as an autonomous therapeutic method, which in itself is capable of giving complete and definite results, has been overlooked. In the records of the section on clinical statistics at the institute directed by the speaker, the number of cases with complete recovery increases daily.

One element in intracavitary aspiration for pulmonary tuberculosis which is still questionable is the draining bronchus; but this has a tendency to lose its importance as a cause of failure.

The special procedure employed for two years in the sanatorium of Naples to influence the last remainder of the cavity and the communicating bronchial passages consists of two stages. First, local antibiotic therapy is practiced to insure the complete cleansing of the remainder of the cavity; second, a fluid consisting of an ethereal solution of iodine is applied locally to exert a sclerosing effect.

Cavity cauterization and irradiation treatment were discussed by Professor Trincas of the University of Ferrara. This method is indicated for the sterilization of the bacterial flora contained in the tuberculous cavities of the lung. The technic includes: roentgenologic or, better, tomographic examination, to localize the cavity; basal anesthesia; local anesthesia; rib resection (3 to 4 cm.), and at intervals of six to eight days opening of the cavity, electrocauterization and use of a quartz lamp for irradiation of the cavity, the period of irradiation to be gradually increased, starting with two or three minutes and increasing to a maximum of twenty minutes.

If the irradiation is performed skilfully, Koch's bacilli disappear in a short time, normally by the tenth irradiation. The practical application of this method has demonstrated that superficial cavities of small and medium size may be eliminated by continuation of irradiation for several months. If one is faced with deep, multiple and giant cavities, the presence of several draining bronchi prolongs and may even prevent elimination of the cavity. In such a case one may proceed with the closure

of the bronchi or, better, with the refilling of the cavity with autoplastic or homoplastic grafts, but only after all exudation has subsided.

It seems advisable to combine this type of treatment with a series of irradiations of the back for a period of several weeks; it seems that these prophylactic irradiations improve the general condition of the patient and hasten healing of the cavity. The presence of fever is not a contraindication; the temperature tends to return rapidly to normal, provided that the period of irradiation is progressively increased two or three minutes per day.

The indications for this type of treatment are not yet well defined. It seems that stationary cavities are more intensively affected by irradiation than cavities still in the phase of development. A large experience will be required to draw definite conclusions as to the type of cases in which cauterization and irradiation should be practiced.

SWITZERLAND

(From a Regular Correspondent)

GENEVA, Jan. 14, 1950.

Research in Rheumatology and Climatology

During the last annual meeting of the Swiss Society for Physical Medicine and Rheumatology, Swiss physicians heard an interesting report from an American physician, Dr. M. Curry, who is now in Bayern (Germany) and whose studies have caused much comment in the German and Swiss medical press. According to Dr. Curry the oxidation power of atmosphere is the essential climatic factor. Under the term "oxidation power of atmosphere," Curry groups ozone and all oxidizing elements of atmosphere, to which he gives the name "aran." High concentrations of "aran" would cause a parasympathicotonic condition with alkalosis and an exaggerated spastic tendency, while low concentrations would provoke a sympathicotonic stimulation, with acidosis of the blood and vascular dilatation, conditions which are favorable to inflammation and hemorrhages. Curry thinks that these two climatic tendencies would correspond to two constitutional types in man. Curry and his collaborators have searched the concentrations of "aran" in many climatic stations and have established a sort of geographic map of these stations, one or another being recommended according to the constitutional type of the patient.

During the same meeting Professor Boni (Zurich) presented a report on the clinical applications of ultrasonics. Interesting therapeutic results have been obtained in rheumatic diseases and in sciatica due to radicular irritability without any syndrome of compression. Tendinous contractions of the "main de Dupuytren" type are also one of the conditions improved by this new treatment. In the articulary diseases, however (e. g., inflammatory arthrosis or chronic arthritis), and in Bechterew's disease there seems to be no real result. However, a geneticist of Zurich who has worked on the fly Drosophila melanogaster has shown the apparition of lethal factors in the chromosomes and of embryonal malformations, forming "phenocopies" similar to these provoked by rubeola embryopathies.

The Swiss Society for Rheumatology, of which Professor Walthard (Geneva) is chairman, and the International Society of Rheumatology will organize an international meeting on rheumatology in Geneva and Zurich in 1953.

Swiss Academy of Medical Sciences

The Swiss Academy of Medical Sciences was founded about five years ago in Basel. Its first chairman was the famous anatomopathologist, Professor Wegelin, whose researches on hyperthyroidism are well known.

The chief aim of the founders of the academy was to coordinate the medical and biologic sciences in Switzerland. The academy is similar to a national council of research with respect to the medical centers of the country, the different faculties of medicine and the physicians. It is based on the principle of free scientific research and does not impose any program of research on the faculties of medicine. Within the limits of its possibilities, the academy tries to give subsidies to research workers in Switzerland and to Swiss workers abroad.

The senate (*Senat*) of the academy is composed of representatives of faculties of medicine and veterinary medicine, medical research workers and specialists in natural sciences useful to medicine. The committee consists of seven members; Professor Miescher, head of the dermatologic clinic of the Zurich University, is chairman. Prof. A. Gigon (Basel), president of the International Society of Internal Medicine, is general secretary.

The academy has separate funds for biology and medicine, allowing young students in these branches to study in Switzerland and abroad and to improve their knowledge in different medical specialties.

Three times a year the academy organizes scientific meetings in different towns of Switzerland. The academy may create expert committees on special problems, like isotopes and genetics in human biology. It can also make grants to many individual research workers for scientific laboratory work or clinical studies.

Under the patronage of the academy, a center for gathering types of microbes has been created in Lausanne, headed by Professor Hauduroy. This center also prepares a catalog and exchanges microbes and viruses.

The official periodical of the academy is the *Bulletin de l'Academie suisse des sciences medicales*, which contains the lectures made in the scientific meetings of the academy and the reports of the expert committees. Each year a book is issued by the academy: the "Bibliographia medica helvetica," which contains a bibliography of all the Swiss medical publications of the year.

The academy has its library, which is a part of the University Library of Basel. The medical heads of the country may find there everything concerning the medical branches and public hygiene of the country.

The academy maintains relations with foreign physicians and experts and has organized a series of international medical meetings.

Experiments with Pituitary Adrenal Corticotropic Hormone in Rheumatoid Arthritis

Dr. R. S. Mach and his collaborators, working in the therapeutic clinic (chief: Professor Bickel) of the Geneva University, have published their first results in the treatment of rheumatoid arthritis with pituitary adrenal corticotropic hormone. The authors have verified Thorn's test by injecting 25 mg. of pituitary adrenal corticotropic hormone into 8 normal subjects: the decrease in eosinophils in all cases was 80 to 100 per cent and the decrease in urinary uric acid-creatinine ratio from 50 to 200 per cent. However, in 5 subjects with Addison's disease, the reduction of eosinophils was not more than 40 per cent and the urinary uric acid-creatinine ratio increased by only 15 per cent.

In 10 subjects with rheumatoid arthritis, the number of eosinophils fell after injection of 25 mg. of pituitary adrenal corticotropic hormone, as is the case in a normal subject, but the urinary uric acid-creatinine ratio did not rise in the usual proportions.

The fact that pituitary adrenal corticotropic hormone produces a rapid clinical improvement and a decrease in eosinophils indicates that in rheumatoid arthritis the endocrine deficiency, if it exists, is not situated in the adrenal cortex but at a higher scale, namely, at the level of the hypophysis or the diencephalon.

A single injection of 25 mg. of pituitary adrenal corticotropic hormone produced in 10 of 12 cases a subjective and objective

improvement which lasted approximately 48 hours. In 1 case the favorable effects lasted 10 days. The 2 patients who did not show any clinical improvement did not show a decrease in eosinophils after an injection of pituitary adrenal corticotropic hormone.

Prolonged treatment by daily injection of pituitary adrenal corticotropic hormone provoked, in 2 patients, a change of clinical state and an improvement of the sedimentation rate. Contrary to what has been published on cortisone, the clinical improvement produced by pituitary adrenal corticotropic hormone was maintained in 2 cases for many weeks after the end of treatment. Because of the inadequate supply of pituitary adrenal corticotropic hormone, the authors use the daily injection of 25 mg. only during the first week of the treatment, continuing then with injections of 6.25 mg. per day, a dosage which is sufficient to maintain the therapeutic action.

TURKEY

(From a Regular Correspondent)

ANKARA, Jan. 12, 1950.

Control of Rabies in Istanbul

The control of rabies in Turkey began in 1887 with the establishment of the Istanbul Antirabic Institute. Prof. Zoeros Pasha of Istanbul University, who had studied under Pasteur in Paris, was its first director and Drs. Remzi and Rifat his associates. Zoeros Pasha generated the virus from rabbits Pasteur himself had inoculated. In the beginning the original Pasteur method was employed and 25 to 30 rabbits per day covered the need, but when, toward the end of World War I, it became difficult to procure rabbits, the more economical Högyes method was resorted to, the Pasteur method being reserved for grave cases. From 1893 to 1896 the institute was directed by Prof. Nicolle and August Marie, until 1914 by Professor Romlinger and then for almost twenty years by his associate Dr. Hayem Naoum and his assistant Dr. Eşref. Since 1932 it has been under the direction of Dr. Zekai Muammer Tuncman, who studied at the Pasteur Institute in Paris. For grave cases, Dr. Tuncman considered the 14 to 20 days of the Högyes method insufficient and supplemented it with the Pasteur-Calmette or the Alivisatos ether method. In 1936 four methods were employed: (1) the Semple vaccine phenol method, (2) the Alivisatos ether vaccine, (3) the Högyes-Philipps method and (4) the August Marie serovaccination method. In grave cases the serovaccine and in less grave or light cases the Högyes-Philipps method modified by the addition of 10 per cent water to the 1:10 glycerin solution.

From 1932 to 1948, of the 33,778 patients receiving prophylactic treatment, 70 (0.2 per cent) died; from 1896 to 1914, of the 6,805 patients, 99 (1.45 per cent) died; from 1914 to 1932, of 6,691 patients, 95 (1.50 per cent) died.

Deaths According to Method of Treatment, 33,778 Patients

Method	No. of Patients	No. of Deaths
Pasteur-Calmette	1,147	20 (1932/1934)
Classic Högyes dilutions	2,304	9 (1932/1934)
Högyes (11 injections)	336	12 (1933)
Semple (5 per cent)	2,683	3 (1933/1934)
Alivisatos	67	4 (1933/1934)
A. Marie (serovaccine)	1,333	19 (1932/1948)
Högyes-Philipps (modified)	25,906	3 (1935/1948)

According to the location of the wounds, their number, depth and size and the kind of animals responsible, the patients were given either the Pasteur-Calmette, the Alivisatos ether or the serovaccine treatment for six days; then the modified Högyes-Philipps method was employed. Of 33,778 persons, 23,894 (70.7 per cent) were bitten by dogs, 4,106 persons (12.2 per cent) by cats, 2,966 (8.7 per cent) by rats, mice or squirrels, 272 by jackals, 134 by wolves, 17 by bears, 4 by hyenas, 2 by badgers and 2,385 by horses, donkeys, oxen, buffaloes or pigs.

Laboratory examination of animals revealed the presence of Negri bodies in the central nervous system of 5,976 (17.7 per cent); 4,063 (12.1 per cent) were reported positively rabic by a physician's or veterinary's clinical observations; 23,739 (70.3 per cent) were unconfirmed; 8,013 (23.7 per cent) were deep

Number of Elapsed Days Before Prophylactic Treatment

No. of Patients	Percentage	No. Elapsed Days
24,930	71.2	0-4
5,325	15.7	5-7
2,967	8.7	8-14
887	2.6	15-21
672	1.8	22-

wounds; 25,765 (76.3 per cent) were superficial; 19,076 (56.4 per cent) were bites on exposed surfaces; 14,702 (43.6 per cent) were bites through the clothing; 2,580 (7.6 per cent) were bites on the head or face; 15,333 (45.3 per cent) on hands and arms; 13,952 (41.3 per cent) on legs, and 1,913 (5.6 per cent) were trunk bites. According to the World Antirabic Institution statistics of Dr. McKendrick of the World Health Organization, the locality percentage of bites on the head and face is 6.5, on hands and arms 39.9, on legs 49.4 and trunk bites 4.2.

According to Dr. McKendrick the first four percentages in table 2 are 64.0, 18.3, 11.8 and 6.0, respectively. In 30 of the 70 patients who died rabies manifested itself during treatment, in 16 (65.7 per cent) within 15 days after completion of treatment and in 24 (34.3 per cent) more than 15 days after treatment. In 30 (42.8 per cent) of the 70 patients death occurred during treatment within 30 days and in 40 patients (57.2 per cent) later than 30 days. Statistics show a decrease in the incubation period of rabies—formerly 24.2 per cent of the deaths occurred during treatment or within 30 days; today the percentage is 42.8. The decrease in incubation period is also noticeable in animals. In 65 (92.8 per cent) of the 70 patients who died of rabies the wounds inflicted were deep and numerous; in 5 (7.2 per cent) they were superficial. Sixty-two bites resulting in death were inflicted on exposed surfaces; 8 bites were effected through the clothing. Fifty-eight of the bites resulting in death were inflicted by dogs, 6 by wolves, 3 by jackals, 2 by hyenas and 1 by a badger. Thirty-five of these 70 patients underwent treatment after a lapse up to 4 days, 17 after 5 to 7 days, 12 after 8 to 14 days, 3 after 15 to 21 days and 3 after 22 days. In the fatal cases, 35 patients (50 per cent) were bitten on the head or face, 30 (42.8 per cent) on the hand or arms and 5 (7.2 per cent) on the legs. There was no fatality among the 1,913 (5.6 per cent) bitten on the trunk, where the bites were probably through the clothing. According to the location of the wounds the fatality rate among the 33,778 persons given the antirabic treatment is as follows: head or face bites 1.35 per cent, bites on hands or arms 0.19 per cent and bites on legs 0.03 per cent. According to Dr. McKendrick's statistics, the percentages are 1.59, 0.26 and 0.15, respectively, and 0.13 per cent fatality from bites on the trunk. In 20 (28.5 per cent) of the animals responsible for the death of the 70 persons, the presence of rabies was confirmed by laboratory examination, 30 animals (42.9 per cent) were reported positively rabic either by a physician or a veterinary; in 20 animals (28.5 per cent) the presence of rabies was unconfirmed because they could not be caught. This indicates that if it is impossible to discover whether or not the animal that inflicted the bite was mad, treatment should be given without delay. The use of strong antirabic vaccines has considerably decreased the death rate of persons bitten by mad dogs. This is also confirmed by Dr. McKendrick's statistics. The death rate from wolf bites, despite prophylactic treatment, was formerly 13.5 per cent, but is now 4.4 per cent. The virulence of the virus is extremely high in wolves and jackals, and the wounds they inflict, mostly on the head and face, are particularly severe and numerous. Despite prophylactic treatment, death is almost

always certain. However, the death rate from rabies contracted through jackal bites has decreased almost as much as that from wolf bites.

Of the 33,778 persons who since 1932 received prophylactic treatment at the Istanbul Antirabic Institute, 25,117 were from Istanbul province, 1,599 from Kocaeli, 1,052 from Bursa and 951 from Tekirdag; Mardin, Erzincan, Tokat, Amasya, Gümüshane, Çoruh, Kirşehir and Mugla each had 2 to 9.

Turkey has now 80 antirabic stations. Exclusive of patients treated at the Ankara, Istanbul and Izmir antirabic institutes, 46,613 persons were given prophylactic treatment from 1933 to 1947. The 67 patients dying of rabies in spite of prophylactic treatment were mostly persons from rural communities who came for treatment after a long lapse or illness was of an extremely grave nature.

Medical Motion Pictures

FILM REVIEW

The Rehabilitation of Laryngectomized Patients. 16 mm., color, sound, showing time sixteen minutes. Prepared in 1949 by LeRoy A. Schall, M.D., Massachusetts Eye and Ear Infirmary, in cooperation with the American Cancer Society. Produced by and procurable on rental or purchase from Sturgis-Grant Productions, Inc., 314 East 48th Street, New York 17.

This motion picture opens with an interview between the surgeon and his patient in which the rehabilitation plans are projected. As the surgeon outlines the various psychologic, educational and social steps that comprise the rehabilitation process, the audience is permitted to see the positive, supporting effect of such early orientation and to anticipate with him what can be done for the patient and, in turn, what must be expected of him in the way of cooperation. The patient is helped to understand that the surgical operation which is to be performed on him will make it impossible for him to speak in the usual way. It also shows the value of immediately giving the patient hope for the recovery of communication through another acceptable route.

The greater part of the film then proceeds to show the patient's earliest relationships with the speech therapist and leads the audience logically through the events of physiologic and psychologic reeducation necessary for speech recovery. The use of group as well as individual technics, the importance of motivated and conscientious practice of new skills and the application of the new method of speaking to life situations are made clear.

It is evident that the film was not designed to provide detailed technical information on speech therapy and mental hygiene but rather to give the viewer an over-all picture of what is involved in establishing adequate communication and vocational rehabilitation in cases in which laryngectomy has been performed. Since it is not intended as a training film for speech therapists or for medical workers, a large number of technical details are omitted and emphasis is placed on the broader principles on which such therapy is based. Probably its greatest value lies in the fact that it presents the persuasiveness and the reasonableness of this method of establishing a "second natural voice" as against rehabilitation by mechanical and electrical prosthesis.

With a few minor exceptions, the information provided in the film as to the nature of the patient's problems and modern methods employed in the solution of these problems is scientifically and clinically accurate. There is reason, however, to question the sequence that shows the mechanics of swallowing air into the stomach since roentgenologic evidence and other methods of study show that the lake or bubble of air in skilful esophageal speakers never goes below the upper third of the esophagus. Speakers who actually swallow air into the stomach are always poor esophageal speakers. It would have been profitable to have had in the film more emphasis on the mental hygience aspect of the rehabilitation of persons who have undergone laryngectomy. It is to be regretted that a number of major problems in the social adjustment of such persons are not made evident.

That complete rehabilitation is not achieved until vocational rehabilitation has been arrived at is a strong note in the film. This film should be useful in medical schools, in speech clinics and for presentation to medical groups, nurses, social workers, professional rehabilitationists and community health groups in general. The photography is excellent.

The Scientific Work of Pasteur. 16 mm., black and white, sound, showing time thirty-three minutes. Produced in 1947 by Marcel Prodotal, Jean Painlevé and Daniel Sorrado. Procurable on rental or purchase from A. F. Films, Inc., 1600 Broadway, New York 19.

This is a biographic film showing some of the best known discoveries in bacteriology made by Pasteur. The character of Pasteur is rather well presented, and the difficulty encountered in meeting the opposition of his contemporaries is clearly shown.

Among Pasteur's achievements portrayed are his proof that there is no spontaneous generation, his findings on fermentation, the discovery of the cause and control of silkworm diseases, sterilization and general use of antiseptics, the relation of Staphylococcus and Streptococcus to infection, control of chicken cholera and anthrax by immunization and his classic discoveries concerning the control of rabies.

The technical nature of this presentation would make it difficult for a person without elementary knowledge of bacteriology and history of science to appreciate Pasteur's accomplishments. It is suitable for high school classes in biology and general science and as a supplement to biology and elementary bacteriology classes in college. It can also be recommended as a valuable introduction to a phase of medical history for premedical students. To the more advanced medical students, it would serve only to supplement their existing knowledge of Pasteur's work.

The substitution of an English sound track in a French picture is a bit disconcerting and at times confusing, though the change in language is well done and with a minimum of loss in meaning. The slow pace of the film could be improved by deletion of some of the repetitious shots of bacterial growth.

This is an excellent documentary picture, illustrating a phase of the early development of bacteriology and its relation to medicine and giving a fair presentation of the personality and works of one of the great men in medical history.

The photography in general is good, and the microcinematography is excellent. The narration is fair.

Elimination. 16 mm., black and white, sound, showing time fourteen minutes. Supervised by Professor Winifred Cullis, C.B.E. Produced in 1949 by Gaumont British Instructional Films, London. Procurable on rental or purchase from United World Films, Inc., 1445 Park Avenue, New York 29.

This film consists of animated diagrams showing how the four major excretory systems cooperate to maintain a constant amount of water in the human body. Beautifully executed drawings show in turn the activities of the sweat glands of the skin, the tubules of the kidney, the air sacs of the lungs and the mucous membrane of the colon in excreting and in reabsorbing water. While many minor technical criticisms could be raised by anatomists, for example, the portrayal of the large intestine, the over-all message of the film is well conveyed, and the student is not confused by an excess of structural or functional detail. A difficult subject is handled discreetly, so that it can be presented to mixed classes without embarrassment to the teacher or students.

The authors missed a few opportunities to present simultaneously the visual and auditory impression of important words, such as cortex, which should have been labeled and pointed out on the screen.

This excellent film on elimination with its fine illustrations and good animation is most suitable for high school and junior college students. It provides a good factual presentation of the four chief methods of elimination. The photography is excellent. The pace of the narration is slow but clear.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS. *Part III.* Boston, Chicago and New York, January. *Parts I and II*, Feb. 13-15. Centers where there are approved medical schools and five or more candidates. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th Street, Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations, July 21. *Oral.* Philadelphia, April 23-27, Chicago, Oct. 8-11. Sec., Dr. Curtis B. Hickcox, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various locations, Feb. 16. *Oral.* Washington, April 14-16. Sec., Dr. George M. Lewis, 66 East 66th Street, New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Boston, April 13-15. San Francisco, June 21-23. The oral examinations in the subspecialties will be held at the same time and places. Asst. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Sec., Dr. W. J. German, 789 Howard Ave., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Oral Part II.* Atlantic City, May 21-28. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1951. Final date for filing applications is July 1, 1950. *Practical.* Boston, May 22-26; Chicago, Oct. 2-6; West Coast, Jan. 1951. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* San Francisco, May, Chicago, October. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: Philadelphia, March 31-April 2; Cincinnati, May 5-7; San Francisco, June 30-July 2. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* Boston, Aug. 26-27. Final date for filing applications is April 1. Sec., Dr. Robert L. Bennett, Georgia Warm Springs Foundation, Warm Springs, Ga.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral.* May-June. Sec., Dr. Louis T. Byars, 4647 Pershing Avenue, St. Louis, Mo.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Spring Examination. Sec., Dr. F. J. Braceland, 103-110 Second Ave., S.W., Rochester, Minnesota.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, week of June 18. Sec., Dr. B. R. Kirklin, 103-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various centers, Oct. 25. Final date for filing applications is July 1. Sec., Dr. J. Stewart Rodman, 225 South 15th Street, Philadelphia.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ALASKA: * Juneau, March 7. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS: * *Examination.* Little Rock, June 8-9. Sec., Dr. Joe Verser, Harrisburg. *Eclectic.* Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main Street, Little Rock.

CALIFORNIA: *Examination, Written.* Los Angeles, Feb. 27-March 2; San Francisco, June 19-23; Los Angeles, Aug. 21-24; Sacramento, Oct. 16-19. *Examination, Oral and Clinical, for Foreign Medical School Graduates.* Los Angeles, Feb. 26; San Francisco, June 18; Los Angeles, Aug. 20; San Francisco, Nov. 12. *Reciprocity, Oral Examinations.* Los Angeles, Feb. 25; San Francisco, June 17; Los Angeles, Aug. 19; San Francisco, Nov. 11. Sec., Dr. Frederick N. Sentens, 1020 N Street, Sacramento 14.

COLORADO: * *Reciprocity.* Denver, April 4. Final date for filing application is March 18. Sec., Dr. George H. Gillen, 831 Republic Building, Denver.

CONNECTICUT: * *Examination.* Hartford, March 14-15. Secretary to the Board, Dr. Creighton Barker, 160 St. Ronan Street, New Haven. *Homeopathic.* Derby, March 9-10. Sec., Dr. Donald A. Davis, 38 Elizabeth Street, Derby.

DELAWARE: *Examination.* Dover, July 11-13. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * *Reciprocity.* Washington, March 13. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: * Jacksonville, June 25-27. Sec., Dr. Frank D. Gray, 12 N. Rosalind Avenue, Orlando.

GEORGIA: *Examination.* Atlanta and Augusta, June. *Endorsement.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: *Endorsement.* Agana, last Friday of each month. Sec., Capt. C. K. Younghin, Dept. of Public Health, Guam, % F.P.O., San Francisco.

IDAHO: Boise, July 10. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: Chicago, April 4-6. Superintendent of Registration, Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: *Examination*, Indianapolis, June. Sec., Dr. Paul R. Tindall, 1138 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Iowa City, June 12-14. Sec., Dr. M. A. Royal, 506 Fleming Building, Des Moines 19.

KANSAS: Kansas City, June 7-8. Sec., Dr. J. F. Hassig, 905 N. 7th Street, Kansas City.

KENTUCKY: *Examination.* Louisville, June 14-16. Sec., Dr. Bruce Underwood, 620 S. 3rd Street, Louisville 2.

MAINE: Portland, March 14-15. Sec., Dr. Adam P. Leighton, 192 State Street, Portland.

MARYLAND: *Examination.* Baltimore, June 20-23. Sec., Dr. Lewis P. Gundry, 1215 Cathedral Street, Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, March 14-17. Sec., Dr. George L. Schadt, 413 E. State House, Boston.

MONTANA: Helena, April 3-5. Sec., Dr. Otto G. Klein, First National Bank Building, Helena.

NEBRASKA: * *Examination.* Omaha, June 5-7. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Building, Lincoln 9.

NEVADA: Carson City, May 1. Sec., Dr. George H. Ross, 112 Curry Street, Carson City.

NEW HAMPSHIRE: Concord, March 8-9. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 20-23. Sec., Dr. E. S. Hallinger, 28 West State Street, Trenton.

NEW MEXICO: * Santa Fe, April 10-11. Sec., Dr. Charles J. McGeey, Coronado Building, Santa Fe.

NORTH DAKOTA: *Examination.* Grand Forks, July 5-7. *Reciprocity.* Grand Forks, July 8. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Reciprocity*, Columbus, April 3. *Examination*, Columbus, June 14-17. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

PUERTO RICO: *Examination.* Santurce, March 7. Sec., Mr. Luis Costo Coll, Box 3717, Santurce.

RHODE ISLAND: * *Examination.* Providence, April 6-7. Chief, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Examination.* Columbia, June 26-29. *Reciprocity.* First Monday of each month. Sec., Dr. N. B. Heyward, 1329 Blanding Street, Columbia.

TEXAS: * *Examination.* Austin, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH. *Examination.* Salt Lake City, June. Dir., Dr. Frank E. Loss, 324 State Capitol Building, Salt Lake City.

VIRGINIA: *Examination.* Richmond, June 23-24. *Endorsement.* Richmond, June 22. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WEST VIRGINIA: Charleston, April 3-5. Sec., Dr. N. H. Dyer, State Capitol, Charleston.

WISCONSIN: * Milwaukee, July 11-13. Sec., Dr. C. A. Dawson, River Falls.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination.* Tucson, March 21. Sec., Mr. Francis A. Roy, Science Hall, University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, May 9. Sec., Mr. L. E. Gebauer, 1002 Donaghey Building, Little Rock.

COLORADO: *Examination*, Denver, March 1-2. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

DISTRICT OF COLUMBIA: Washington, April 17-18. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Building, Washington.

FLORIDA: *Examination.* June 3. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

IOWA: *Examination.* Des Moines, April 11. Sec., Dr. Ben H. Petersen, Coe College, Cedar Rapids.

MINNESOTA: *Examination.* Minneapolis, April 4-5. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, May 2-3. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.

OKLAHOMA: *Examination.* Oklahoma City, April 11. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

SOUTH DAKOTA: Vermillion, June 3-3. Sec., Dr. Gregg M. Evans, 310 E. 15th Street, Yankton.

TENNESSEE: *Examination.* Memphis, March 17-18. Sec., Dr. O. W. Hyman, 874 Union Avenue, Memphis.

TEXAS: *Examination.* Austin, April 21-22. Sec., Brother Raphael Wilson, 306 Nalle Building, Austin.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1939 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 10 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Annals of Surgery, Philadelphia

130:289-592 (Sept.) 1949

Mission Accomplished: Task Ahead. F. W. Rankin.—p. 289.
Cancer of Breast. H. G. Bell.—p. 310.
*Malignant Melanoma: 40 Cases Treated by Radical Resection. W. S. McCune.—p. 318.
Development of New Methods for Histochemical Demonstration of Hydrolytic Intracellular Enzymes in Program of Cancer Research. A. M. Seligman, M. M. Nachlas, L. H. Manheimer and others.—p. 333.
Surgical Treatment of Congenital Pulmonary Stenosis. W. J. Potts.—p. 342.
Experimental Evaluation of Certain Methods of Suturing Thoracic Aorta. Y. Sako, T. C. Chisholm, K. A. Merindino and others.—p. 363.
Surgical Relief of Congestion in Pulmonary Circulation in Cases of Severe Mitral Stenosis: Preliminary Report of 6 Cases Treated by Means of Anastomosis Between Pulmonary and Systemic Venous System. R. H. Sweet and E. F. Bland.—p. 384.
Valsalva Maneuver: Aid for Contrast Visualization of Aorta and Great Vessels. N. E. Freeman, T. M. Fullenlove, E. J. Wylie and R. S. Gilhillan.—p. 398.
Surgical Treatment of Insidious Thrombosis of Aorta: Report of 10 Cases. D. C. Elkin and F. W. Cooper Jr.—p. 417.
Quantitative Studies on Time Factor in Arterial Injuries. H. H. Miller and C. S. Welch.—p. 428.
Clinical Evaluation of Two Tests for Incipient Thrombosis: Prothrombin Activity and Fibrinogen B of Lyons. R. D. McClure, C. R. Lam, J. Barron and R. R. Margulis.—p. 439.
*Physiologic Studies in Cases of Stricture of Common Bile Duct. W. Walters.—p. 448.
*Intrahepatic Cholangiojejunostomy for Biliary Obstruction—Further Studies: Report of 4 Cases. W. P. Longmire Jr. and M. C. Sanford.—p. 445.
Deperitonealization: Clinical and Experimental Observations. G. F. Robbins, A. Brunschwig and F. W. Foote.—p. 466.
Intestinal Obstruction in Newborn. D. M. Glover and F. McA. Barry.—p. 480.
Gastro-Intestinal Gas: Observations on Belching During Anesthesia, Operations and Pyelography; and Rapid Passage of Gas. W. G. Maddock, J. L. Bell and M. J. Tremaine.—p. 512.
Sphincter-Preserving Operations for Rectal Carcinoma as Related to Anatomy of Lymphatics. R. R. Best and J. B. Blair.—p. 538.
Extension of Carcinoma of Stomach into Duodenum and Esophagus. M. M. Zinninger and W. T. Collins.—p. 557.
End Results of Complete Versus Intracapsular Removal of Acoustic Tumors. G. Horrax and J. L. Poppen.—p. 567.
Streptomycin, Aureomycin and Chloromycetin: Experimental and Clinical Comparison. G. H. Yeager, W. L. Byerly Jr. and W. A. Holbrook Jr.—p. 576.

Malignant Melanoma.—McCune reports observations on 40 cases of malignant melanoma treated by surgical extirpation and radical nodal dissection at Walter Reed General Hospital from 1942 to 1946, inclusive. In most instances the melanoma had been removed elsewhere, often at an overseas installation, the patient being transferred to this hospital because of a malignant growth in the lesion. Treatmen: consisted in review of the transfer slide, if available, followed by radical resection of the lymph nodes draining the area involved. The nodes were resected, whether or not they were palpably enlarged. In many instances the original scar was excised and a strip of skin and fascia between it and the lymph nodes removed en bloc. All cases were divided into two groups, depending on the presence or absence of palpable lymph nodes. There were 25 cases in which glandular enlargement was present on admission, 12 in which it was absent and 3 in which records were incomplete. Among the 12 cases in which no palpable adenopathy was present at the time of the lymph node resection, 7 showed evidence of metastasis in the nodes removed. All 7 patients were alive at the time of reporting, without evidence of further metastasis or recurrence, one to six years postoperatively. Of 5 patients without palpable adenopathy or pathologic evidence of metastasis in the nodes removed, 1 died of distant metastases four months after operation. The remaining 4 patients were alive and well at the time of reporting, one to three years following resection. Only 2 of 25 patients in whom nodular enlargement was present at time of operation did not present evidence of metastasis in the nodes removed. One of these patients was alive and well two years and nine months after the operation; one showed roentgenographic evidence of a metastatic lung tumor two years and six months after resection. Of the remaining 23 patients with palpable adenopathy and pathologic evidence of metastasis, 20 were dead, 18 having died within two years after the operation. One was alive with metastases one year after operation; 2 were alive and well two to three years after operation. These results demonstrate the importance of early radical resection of regional lymph nodes, whether or not they are enlarged, whenever a diagnosis of malignant melanoma is made.

Stricture of Common Bile Duct.—Since 1924 Walters has operated on 186 patients for stricture of the extrahepatic bile ducts. The considerable reduction in the mortality rate in the patients treated since 1940 can be attributed to a better understanding of the pathologic physiology of the liver in cases of biliary obstruction and the institution of adequate methods of treatment before, during and after operation in order to compensate for the disturbances. Prevention of bleeding has been accomplished by the administration of vitamin K and blood. As a result, the syndrome of hepatorenal insufficiency does not occur. More diligent search for both ends of the duct beyond the stricture has been productive of a greater percentage of cases in which anastomosis of duct to duct or duct to the duodenum could be accomplished. Evidence indicates that after a biliary-duodenal anastomosis, reflux of food (barium or air) into the common and hepatic ducts is not responsible for pain, fever or jaundice but that these symptoms are the result of recurring obstruction of varying degree at the site of the previously made anastomosis. This is important because of the simplicity and ease of these operations in comparison to the operation needed to anastomose the duct to the jejunum, especially if the Roux-Y principle of jejunal anastomosis is used. Studies are under way to determine whether results of anastomosing the ends of the duct are as good, better or worse than those of anastomosing the proximal end of the duct to the duodenum. Involved in this problem is the fact that concentric contraction occurs at the site of most circular or tubular ductal anastomoses unless prevented by a tubular prosthesis until the usual period of such contracture has passed. To prevent contracture of a circular biliary ductal anastomosis, a rubber catheter extending from the hepatic duct into the duodenum may be used as a splint. The catheter, which will be pulled into the duodenum by peristalsis, can be maintained in position by a silk suture passing through it and brought out to the skin, where it is anchored to a button as advised by McArthur. Other short tubes, even of vitallium, placed within the duct will have their lumens plugged and obstructed by bile, and bile will accumulate about them. This foreign body will obstruct the common duct unless removed, for they will not pass through the sphincter of Oddi. Hence they should not be used.

Intrahepatic Cholangiojejunostomy.—In 1948 Longmire and Sanford described an anastomosis of one of the intrahepatic biliary ducts to the jejunum following a partial resection of the left lobe of the liver for extensive benign strictures of the extrahepatic biliary system. The procedure was suggested for cases in which the usual methods of biliary reconstruction had proved inadequate. Experimental studies and a report of a case in which this method was used successfully were presented. Three additional patients have since been treated by this procedure. The authors review their experiences with this method in 4 adults in whom extensive benign biliary obstruction recurred as a result of failure of the usual methods of biliary reconstruction. In all cases it was technically possible to perform a satisfactory cholangiojejunal anastomosis. In the selected cases in which the procedure was indicated it had three advantages over the usual methods of repair: 1. Less scarring and fewer adhesions were encountered in the left upper part of the abdomen than in the right. 2. After exposure of the intrahepatic duct its superficial position in relation to the anterior abdominal wall facilitated the performance of an accurate anastomosis with the jejunum. 3. There were not any vital structures to be avoided in the

immediate operative area, such as the portal vein and the hepatic artery. One patient had been well for eleven and a half months following operation. Two patients have been greatly improved but have had intermittent difficulties related to the abnormality of the biliary tract. One patient died three months after operation as a result of homologous serum hepatitis. He had recovered from operation and was well at the time of onset of the fatal illness. The procedure should be considered in certain cases of extensive destruction of the extrahepatic biliary system if previous reconstructive procedures have failed.

Archives of Dermatology and Syphilology, Chicago

60:475-640 (Oct.) 1949

Present Status of Dermatologic Training in the United States. F. E. Senear, G. M. Lewis and F. E. Cormia.—p. 475.
Survey of Tinea Capitis, Including Favus. J. H. Swarts, E. M. Rockwood and E. A. Glicklich.—p. 486.
Hypertrophic Darier's Disease and Nevus Syringocystadenomatosus Papilliferus: Histopathologic Study. H. Beerman.—p. 500.
Essential Hirsutism: Dermatologic and Endocrinologic Considerations. J. L. Callaway, J. T. Wortham, E. C. Hamblen and A. A. Salmon.—p. 528.
*Treatment of Neurosyphilis with Penicillin Combined with Artificial Fever. N. N. Epstein and J. M. Key.—p. 543.
Paralysis of Cranial Nerves Complicating Herpes Zoster. M. J. Costello and M. J. Scott.—p. 558.
*Relapsing Febrile Nodular Panniculitis (Weber-Christian Disease): Review of Literature and Report of Case. W. L. Bendel Jr.—p. 570.
Enhancing Photodynamic Effect of Solutions of Crude Coal Tar on Skin. L. Frank—p. 597.
Supernumerary Ears: Report of 3 Cases. C. S. Miller and K. F. Miller.—p. 601.
Lipomelanotic Reticulosis of Lymph Nodes in Case of Lichen Planus. M. E. Obermayer and E. T. Fox.—p. 609.
Treatment of Lupus Vulgaris with Calciferol (Vitamin D2). H. Pariser and J. W. Anderson.—p. 614.

Treatment of Neurosyphilis.—Epstein and Key treated 87 patients with various types of neurosyphilis with penicillin combined with artificial fever therapy. Penicillin was administered in two forms: (*a*) aqueous penicillin sodium, intramuscularly, every three hours around the clock for fourteen days, for a total dose of 4,500,000 units and (*b*) penicillin calcium suspended in peanut oil containing 4.5 per cent white wax U. S. P., administered in daily single intramuscular injections of 300,000 units each for twenty days, for a total of 6,000,000 units. Artificial fever therapy was administered by the blanket method during and after the penicillin course. Five hours of a temperature over 104 F. was considered a single treatment. Most of the patients received a total of fifty hours of fever therapy. Fifty-five of the 87 patients have been followed from 120 to 365 days and 23 for longer periods. The clinical response in the patients with dementia paralytica and meningovascular neurosyphilis was satisfactory. Little change in the clinical condition was noted in those with tabes dorsalis. Definite improvement in the spinal fluid signs was noted in 37 of 55 patients (70 per cent) during the first year of post-treatment observation and in 20 of 23 patients (87 per cent) observed for a longer period. The cell count, protein content and colloidal gold reaction of the spinal fluid had a tendency to reverse to normal promptly. The Wassermann reaction was not as satisfactory. The reactions to serologic tests of the blood became negative in only 7 patients (14.5 per cent) during the first year of observation. This percentage did not change during the second year of observation. Two severe Herxheimer reactions in the central nervous system were observed. A rise in temperature during the first twenty-four hours of aqueous penicillin sodium therapy was noted in 14 of 28 patients so treated. The fever therapy was well tolerated by all but 2 patients. The authors had better results with the combination of penicillin and fever therapy than with chemotherapy combined with fever therapy. Penicillin therapy of neurosyphilis, although superior to any other single therapeutic procedure, has its limitations.

Nodular Panniculitis.—Bendel reports 1 case of relapsing febrile nodular panniculitis, or Weber-Christian disease, in a woman aged 35, and an analysis of 43 cases of the disease in 33 women and 10 men mentioned in the literature. In only 9 of the cases were the patients less than 20 years old, and only 3 of them were infants. Relapsing febrile nodular panniculitis is characterized by recurring bouts of fever, associated with the appearance of crops of subcutaneous nodules, varying from the size of a pea to several inches in diameter, usually on the thighs and arms and frequently on the abdomen, back and legs. The nodules, which may be either painless or tender to touch, are frequently erythematous and raised above the surface of the normal skin. The pathologic changes appear to be necrosis of the subcutaneous fat, with infiltration by lipophages and eventually fibrosis. The nodules may slowly regress over a period of months, leaving shallow or deep-pitted areas covered by normal skin. As a rule, no pathologic changes are observed in the other body systems, although death from the disease per se has been reported in 4 cases. In a few cases an enlarged spleen and leukopenia have been outstanding features. Although the cause is unknown, the clinicopathologic features suggest that panniculitis of the Weber-Christian type is a syndrome rather than a disease entity. It is the result of some noxious stimulus producing a metamorphosis in the subcutaneous fat, and possibly also in the visceral fat in the severer cases, the fat acting as a foreign body and calling forth a foreign body response, with the reticuloendothelial system playing a large part in the syndrome. The mechanism may be in the form of a nonspecific type of allergy. General systemic measures, local massage and heat and a trial of the sulfonamide compounds, in adequate dosage, or penicillin appear to offer the best outlook.

Archives of Internal Medicine, Chicago

84:523-666 (Oct.) 1949

Symptoms Attributable to Cold Hemagglutination: Report of 2 Cases. J. C. Bateman.—p. 523.
Ulcer of Pyloric Ring: Report of 20 Cases. G. A. Boylston.—p. 532.
Spontaneous Rupture of Syphilitic Saccular Aneurysms of Ascending Aorta into Pericardial Cavity with Hemopericardium: Report of Sudden Death in 29 Cases. P. Goldstein.—p. 540.
Dissecting Aneurysms of Aorta. J. G. Schlichter, G. D. Amromin and A. J. L. Solway.—p. 558.
Hematologic Studies in Hiroshima and Control City Two Years After Atomic Bombing. F. M. Snell, J. V. Neel and K. Ishibashi.—p. 569.
Clinical Significance of Bacteroides. P. M. Beigelman and L. A. Rantz.—p. 605.
Myocardial Infarction: Observations on 100 Patients Who Survived up to Six Years. G. Y. Mills, A. J. Simon, F. Cisneros and L. N. Katz.—p. 632.
Intravenous Catheterization of Heart in Suspected Congenital Heart Disease: Report of 72 Cases. D. W. Chapman, D. M. Earle, L. J. Gugle and others.—p. 640.

Archives of Otolaryngology, Chicago

50:373-512 (Oct.) 1949

Surgery at Base of Tongue by Transpharyngeal Approach. G. Portmann.—p. 373.
Perilymph: Its Relation to Improvement of Hearing Which Follows Fenestration of Vestibular Labyrinth in Clinical Otosclerosis. J. Lempert, E. G. Wever, M. Lawrence and P. E. Meltzer.—p. 377.
Suggestions for Speech Reception Testing. J. D. Harris.—p. 388.
Virus Vaccine Immunization Against Common Cold. N. Fox and G. S. Livingston.—p. 406.
Use of Radium in Treatment of Hypertrophic Lymphoid Tissue in Nasopharynx. C. H. Dow.—p. 417.
Abscess of Cerebellar Lobe of Otogenic Origin: Combined Otolaryngologic and Neurosurgical Treatment in 6 Cases. J. X. Medwick, A. Uihlein and O. E. Hallberg.—p. 429.
Tinnitus Aurium in Otosclerosis. M. Saltzman and M. S. Ersner.—p. 440.
Review of Allergy for 1947. E. L. MacQuiddy and E. A. Holyoke.—p. 466.

Arizona Medicine, Phoenix

6:1-76 (Sept.) 1949

*Congenital Pulmonary Cysts. T. B. Wiper.—p. 21.
Symptoms of Dizziness. K. M. Simonton.—p. 28.
Recurrent Pancreatitis. H. D. Cogswell.—p. 33.
Principles of Parenteral Fluid Administration. R. J. Jennett.—p. 35.

Congenital Pulmonary Cysts.—Wiper reports 10 cases of congenital pulmonary cysts in 6 men between the ages of 21 and 51, 2 women aged 24 and 31 and 2 baby girls aged 1½ month and 4½ months. The cysts manifested themselves in 3 of the male patients by a superimposed suppurative infection on the already physiologically impaired respiratory function due to the presence of congenital cysts. Pulmonary cysts with bronchial communications are more apt to present clinical symptoms than those without communication, because of the increased susceptibility to suppurative disease and cough with the production of large amounts of mucopurulent sputum. Cough, mucopurulent expectoration, chest wall pain, febrile illnesses, hemoptysis and dyspnea are frequently associated with pulmonary cysts. The 2 infants and 1 woman had isolated

balloon type cysts of congenital bronchial pulmonary origin expressing themselves in dyspnea. Thoracotomy was performed on all the patients and was followed by lobectomy in 6 and by pneumonectomy in 1. The treatment of congenital pulmonary cysts is best accomplished by surgical excision of the cyst itself or the cyst and the associated lobe of the lung, if conservation of lung tissue cannot be accomplished.

Bulletin of Johns Hopkins Hospital, Baltimore

85:183-252 (Sept.) 1949

Diagnosis of Portal Vein Obstruction; Studies of Intestinal Absorption of Glucose Using Abdominal Collateral Veins. F. T. Billings Jr. and H. E. DePree.—p. 183.
Treatment of Cutaneous Carcinoma with Podophyllin: Preliminary Note. M. Sullivan.—p. 200.
Comparison of Sarcoidosis and Tuberculosis with Respect to Complement Fixation with Antigens Derived from Tubercle Bacillus. W. H. Carnes and S. Raffel.—p. 204.
Clinical Therapeutic Trial of New Drug. E. K. Marshall Jr. and M. Merrell.—p. 221.
Studies on Initiation of Blood Coagulation: I. Relationship of Platelets to Clot-Promoting Effect of Glass Surfaces. R. C. Hartmann, C. L. Conley and J. S. Lalley.—p. 231.

Cancer, New York

2:755-942 (Sept.) 1949. Partial Index

Results of Pancreatoduodenectomy. A. Brunschwig.—p. 763.
Palliative Resections in Cancer of Colon and Rectum. J. Modlin and H. S. J. Walker.—p. 767.
Significance of Cartilage in Abnormal Locations. B. L. Coley and N. L. Higinbotham.—p. 777.
Osteogenic Sarcomas with Multiple Skeletal and Visceral Involvement. B. Halpert, P. E. Russo and V. C. Hackney.—p. 789.
Benign Chondroblastoma of Bone: Unusual Localization in Femoral Capital Epiphysis. L. Lichtenstein and L. Kaplan.—p. 793.
Argentaffin Tumor Recurring in Benign Cystic Teratoma of Ovary. N. Mitchell and B. Diamond.—p. 799.
Primary and Metastatic Cancer of Fallopian Tube. W. F. Finn and C. T. Javert.—p. 803.
Bilateral Primary Carcinoma of Ureter: Case Report. R. K. Ratliff, W. C. Baum and W. J. Butler.—p. 815.
Carcinoid Tumors of Colon and Rectum. R. C. Horn Jr.—p. 819.
Vaginal Smear as Means of Investigating Early Carcinoma of Cervix. O. Gates, J. C. MacMillan and M. Middleton.—p. 838.
*Limitations of Cytological Diagnosis of Malignant Tumors. J. H. Ferguson.—p. 845.
Electron-Microscopy Observations on Hodgkin's Material. J. A. Jacques and K. R. Porter.—p. 853.
Reversal of Aminopterin-Induced Inhibition of Sarcoma 180 by Folic Acid. A. Goldin, B. Goldberg, L. G. Ortega and E. B. Schoenbach.—p. 857.
Bone-Marrow Changes in Man After Treatment with Aminopterin, Amethopterin and Aminoanfol, with Special Reference to Megaloblastosis and Tumor Remission. I. B. Thiersch.—p. 877.

Limitations of Cytologic Diagnosis of Malignant Tumors.—Ferguson points out that changes in nuclear size, shape and staining characteristics that are regarded as characteristic of malignant tumors occur also in many nutritional, degenerative or inflammatory reparative processes. Reliance on these changes alone, in a single or few cells in sections or smears, for the diagnosis of a malignant tumor will lead to a high rate of false positive diagnoses. These limitations must be recognized by both clinicians and pathologists. Examination of smears for the diagnosis of possible presence of a malignant tumor is only an adjunct, and it must be realized that other diagnostic procedures are needed.

Delaware State Medical Journal, Wilmington

21:189-222 (Sept.) 1949

Tuberculosis Morbidity and Mortality in Delaware. L. D. Phillips and G. T. Evans.—p. 189.
Public Health Nursing Functions in Tuberculosis Control Program. M. M. Klaer.—p. 190.
Cancer Program of State Board of Health: Report No. 3. J. W. Spies.—p. 192.
Private Physician Takes Over Venereal Disease Control. W. L. Porter.—p. 196.
Marriage Trends. C. A. Marshall.—p. 197.
Nutrition in Pregnancy. M. T. Davenport.—p. 200.
Vital Points of Delaware Premarital Law. R. D. Herdman.—p. 201.
Are Our Children Protected Against Diphtheria and Smallpox? Report on Immunization Status of 6 Year Old Children in Kent County. C. R. Hayman.—p. 203.
Expansion of Crippled Children's Services in Delaware Under State Board of Health. C. P. Knight.—p. 206.
Value of Early Recognition of Congenital Defects. M. L. McCarthy.—p. 209.
Fluorine Program in Delaware. M. H. Jeffreys.—p. 210.

Gastroenterology, Baltimore

13:111-204 (Aug.) 1949

*Carcinoma of Pancreas, Clinical and Pathologic Study of Seventy-Five Cases. A. Arkin and S. W. Weisberg.—p. 118.
Response of Serum Amylase and Lipase to Pancreatic Stimulation as Test of Pancreatic Function: Mecholyl-Secretin and Morphine-Secretin Tests. J. Myhre, S. Nesbitt and J. T. Hurly.—p. 127.
External Pancreatic Secretion as Measured by Secretin Test in Patients with Idiopathic Steatorrhea (Nontropical Sprue). M. W. Comfort, G. R. Dornberger, E. E. Wollaeger and M. H. Power.—p. 135.
Concurrence of Migraine and Peptic Ulcer. M. S. Kleckner Jr. and B. T. Horton.—p. 141.
*Management of Massive Esophageal Hemorrhage with Tamponade and Thrombin. C. B. Barnett and S. Cohen.—p. 144.
Diagnosis of Carcinoma of Esophagus: Method of Biopsy with Retrograde Curette. A. B. Crump and G. C. Henning.—p. 153.
Mesenteric Lymphadenitis: Clinical and Experimental Study. D. R. Webster and P. Madore.—p. 160.

Carcinoma of Pancreas.—According to Arkin and Weisberg carcinoma of the pancreas accounts for 6 per cent of cancers of the abdominal organs. They review observations in 75 cases of carcinoma of the pancreas in which necropsy was performed at Cook County Hospital in Chicago during a ten year period. Early diagnosis of pancreatic malignant tumors has become more important since the recent advances in the surgical treatment of these tumors. The possibility of carcinoma of the pancreas must be considered when a patient presents a history of abdominal pain which is not due to peptic ulcer, gallstones or renal colic, and is associated with a progressive and rapid loss of weight, with or without jaundice. The old concept of a painless progressive jaundice as the typical symptom complex of pancreatic carcinoma is incorrect, as most patients do have pain and many do not have jaundice. In this series of 75 cases 37 tumors occurred in the head of the pancreas, 12 in the body, 16 in the tail, 8 in the body and tail, and 2 in aberrant pancreatic tissue. The pain, present in 85 per cent of cases of pancreatic malignant tumor, may be mistaken for that of spondylitis, intercostal neuralgia, calculus, gallbladder disease or peptic ulcer. It may radiate from the epigastrium to the back, to the right or left upper abdominal quadrant or downward toward the groin. An important characteristic is the variation in intensity with change of position. Many patients prefer to sit or lean forward. They may lie with the body curled, on the right or left side. The pain may be paroxysmal, without relation to the intake of food. It is often dull and boring. It is frequently combined with nervous manifestations, such as anxiety, and some patients are given the diagnosis of psychosis. Carcinoma of the pancreas should be considered when there is a rapid loss of weight not due to diabetes, hyperthyroidism, tuberculosis, anorexia nervosa, sprue or gastrointestinal malignancy. Anorexia occurred in most of the patients. Constipation is much more frequent than diarrhea. Icterus was present in only 37 of 75 cases. The chief clinical findings were a palpable liver, palpable tumor mass, jaundice, palpable gallbladder and ascites. Roentgenographic study is helpful in 40 per cent of cases. Gastric and prepyloric defects, duodenal distortion or defect, displacement of the transverse colon downward, obstruction of the pyloric region or duodenum or filling defects simulating primary tumor of the stomach, duodenum or colon may occur. The stools are often clay colored. The serum alkaline phosphatase is usually elevated above 15 Bodansky units. The serum total cholesterol may be increased above 300 mg. per hundred cubic centimeters. Hyperglycemia is a valuable finding. It is present in 25 to 50 per cent of cases. True diabetes may develop with extensive destruction of the islet tissue. Blood amylase and lipase may be increased.

Management of Massive Esophageal Hemorrhage.—Barnett and Cohen report 4 cases of massive esophageal bleeding satisfactorily treated with tamponade. Previously Rowntree and co-workers, as well as Tocantins, had reported on intra-esophageal tamponade in bleeding esophageal varices by means of an inflated balloon attached to a double lumen tube. A Miller-Abbott tube may be employed. The authors passed a Miller-Abbott tube transnasally into the stomach and distended it with water containing 20 cc. of iodopyracet injection. The amount of water needed for satisfactory compression varies with the type of tube and should be ascertained by a trial

filling before passage. The water-filled bag exerts adequate tamponade. The radiopaque fluid permits radioscopic control of the balloon's position. The tube is then gently pulled up against the cardia until a definite resistance is encountered. To prevent slipping, the external tubing is secured against the upper lip with adhesive. A roentgenogram or fluoroscopy should reveal the upper pole of the bag at the juncture of cardia and esophagus. Aspiration of the gastric contents at regular intervals should help detect recurrent hemorrhage. Between twenty-four and seventy-two hours should be sufficient time to establish satisfactory hemostasis. Although intermittent decompression has been suggested to prevent necrosis of the mucosa, the authors maintained tamponade for as long as seventy-two hours without subsequent pressure necrosis. Because of an experience with recurrence of hemorrhage in one of their cases after the removal of the tube, they now deflate the balloon at the end of the period of tamponade and slip the tube into the antrum for a further twelve to twenty-four hour period. Thus, if repeated suction should reveal renewed bleeding, reestablishment of tamponade can be quickly achieved. In 3 of their 4 patients the authors combined esophageal tamponade with the topical application of thrombin. A solution of 10 cc. of water may be sipped or, if the patient is comatose, slowly instilled through a Levine tube temporarily placed in the upper esophagus. The tampon should prevent the too rapid passage of the thrombin past the cardia, and the "bleeder" thus might be bathed in a strongly hemostatic solution. The patient should be in Fowler's position to prevent aspiration. During the first twenty-four hours the thrombin may be used every four to six hours.

Journal of Clinical Investigation, Cincinnati

28:821-1056 (Sept. [Part 1]) 1949. Partial Index

SYMPOSIUM ON ANTIBIOTICS

Studies on Hypersensitivity to Penicillin. I. Incidence of Reactions in 1,303 Patients. M. H. Lepper, H. F. Dowling, J. A. Robinson and others.—p. 826.
Recovery of Bacteria from Toxic Effects of Penicillin. H. Eagle.—p. 832.
Development of Resistance of Salmonella Typhosa to Fatty Acid Salts of Streptomycin and Dihydrostreptomycin. H. Welch, H. Pinchbach, C. W. Price and C. H. Shaffer.—p. 856.
Effects of Normal Horse Serum on In Vitro Activity of Tyrothricin. R. J. Reedy and S. W. Wolfson.—p. 861.
In Vitro Studies on Possible Synergistic Action Between Penicillin and Bacitracin. M. C. Bachman.—p. 864.
Comparison of Action of Streptomycin, Polymyxin B, Aureomycin and Chloromycetin on H. Pertussis, H. Parapertussis, H. Influenzae and Five Enteric Strains of Gram-Negative Bacilli. H. E. Alexander, G. Leidy and W. Redman.—p. 867.
Experimental Studies on Action of Streptomycin, Aureomycin and Chloromycetin on Brucella. E. M. Yow and W. W. Spink.—p. 871.
Patterns of Bacterial Resistance to Penicillin, Aureomycin and Streptomycin. M. Demerec.—p. 891.
Partial Purification and Properties of Antibiotic Substances from Sweet Potato Plant (Ipomoea Batatas). B. N. Bruckner, H. H. McKay, P. S. Schaffer and T. D. Fontaine.—p. 894.
Partial Purification and Properties of Antibiotic Substances from Banana (Musa Sapientum). W. E. Scott, H. H. McKay, P. S. Schaffer and T. D. Fontaine.—p. 899.
Lupulon and Humulon—Antibiotic Constituents of Hops. J. C. Lewis, G. Alderton, J. F. Carson and others.—p. 916.
Occurrence of Antibacterial Substances Active Against Mycobacterium Tuberculosis in Seed Plants. R. Y. Gottshall, E. H. Lucas, A. Liehfeldt and J. M. Roberts.—p. 920.
Neomycin—Production and Antibiotic Properties. S. A. Waksman, H. A. Lechevalier and D. A. Harris.—p. 934.
Chloramphenicol (Chloromycetin), Antibiotic. Pharmacological and Pathological Studies in Animals. O. M. Gruhzit, R. A. Fisken, T. F. Reutner and E. Martino.—p. 943.
Beneficial Effect of Chloromycetin in Brucellosis. T. E. Woodward, J. E. Smadel, W. A. Holbrook and W. T. Raby.—p. 968.
Effect of Aureomycin Against Bacterium Tularense. J. C. Ransmeier.—p. 977.
*Clinical Evaluation of Aureomycin. H. Brainerd, E. H. Lennette, G. Meiklejohn and others.—p. 992.
*Further Experiences with Intravenous Aureomycin Therapy. Study of 116 Cases. M. Sanders, J. M. Rumball, C. Solomon and others.—p. 1006.

Clinical Evaluation of Aureomycin.—Brainerd and his associates used aureomycin in the treatment of 116 patients with infections due to a variety of bacterial, rickettsial and viral agents. Adult patients taking aureomycin by mouth were given 1 Gm. every four to eight hours. The only significant toxic symptoms encountered frequently were nausea and vomiting. The intravenous route of administration, used in 68 persons, proved to be an effective method of therapy, when used to supplement oral medication to produce high serum concentrations of aureomycin or to replace the oral route in the control of nausea and vomiting. Aureomycin appeared to exert beneficial effect in acute brucellosis, leptospirosis, Q fever, primary atypical pneumonia, psittacosis, chancroid, lymphopathia venereum, generalized peritonitis and many infections of the urinary tract. Beneficial effects from aureomycin therapy appeared to be limited or absent in typhoid, Salmonella and Shigella infections, coccidioidal pneumonia, infectious mononucleosis, varicella and subacute bacterial endocarditis due to Streptococcus fecalis.

Intravenous Aureomycin Therapy.—Sanders and associates say that the need for developing routes of administration for aureomycin other than oral has been apparent since the initial clinical trials. They report observations on 116 patients who were given aureomycin intravenously. They report studies on blood concentrations and urinary excretions under several intravenous-oral and oral dosage schedules. Absorption of aureomycin in the blood appears to vary with the individual patient. Carinamide may enhance blood levels of aureomycin and it definitely decreases excretion of the antibiotic through the kidneys. No serious toxic effects have been noted following intravenous aureomycin therapy. Only 2 of the 116 patients experienced febrile reactions. These reactions appeared to be of an individual nature, since the same production lots failed to evoke reactions in other patients. With the preparation of aureomycin now available, phlebitis occurred in 30 to 40 per cent of the patients when the antibiotic was given intravenously. Nausea and vomiting were not encountered as direct concomitants of intravenous therapy. Gastrointestinal symptoms were not noted even in a patient who had received 76 injections of 500 mg. by vein.

Southern Surgeon, Atlanta, Ga.

15:545-658 (Aug.) 1949

Successful Embolectomy at Bifurcation of Aorta. J. P. Wolff.—p. 545.
Carcinoma of Breast Occurring During Pregnancy or Lactation: Report of 12 Cases. J. M. Parker and W. M. Aldredge.—p. 550.
Clinical Pathologic Conference. B. Halpert and J. M. Parker.—p. 555.
Paralytic Ileus. G. E. Stambro.—p. 562.
Experiences with Spool Cotton Suture Material. H. C. Dodson Jr. and H. A. Burnett.—p. 571.
Injuries of Larynx and Trachea. J. F. Burton and H. M. Anderson.—p. 579.
Primary Carcinoma of Lung. E. Fair.—p. 584.
Traumatic Strictures of Extrahepatic Biliary Ducts. C. M. O'Leary and W. T. Snoddy.—p. 595.
Pseudomonas Infection of Mandible with Discussion and Case Report. F. J. Reichmann, G. E. Reynolds Jr. and H. F. Marsh.—p. 606.
Surgical Treatment of Thyroid Disease. F. M. Lingenfelter and R. B. Howard.—p. 611.
Carcinoma of Jejunum: Brief Discussion and Case Report. A. H. Bell and H. M. Richey.—p. 616.
Congenital Pyloric Stenosis. E. B. Neff.—p. 623.
Acute Obstruction of Small Bowel. E. M. Farris.—p. 628.
Place of Patellectomy in Treatment of Fractures of Patella. D. H. O'Donoghue.—p. 640.

Texas State Journal of Medicine, Fort Worth

45:613-668 (Sept.) 1949

Diabetes Mellitus—Orientation. C. Striker.—p. 617.
Neglected Diabetic Patients. J. S. Sweeney.—p. 623.
Diabetes Mellitus and Pregnancy. O. V. Prejean and J. B. Griffin.—p. 627.
Doctor in His Relationship to the Community. W. L. Pressly.—p. 630.
Preoperative Management of Jaundiced Patient. F. J. Kelly.—p. 633.
Recent Advances in Chemical Supportive Therapy of Thermal Injury. C. A. Moyer.—p. 635.
New Antibacterial in Surgery: Sulfamylon-Streptomycin. W. R. Whitehouse, R. W. Kimbro and G. R. Wright.—p. 639.
Diaphragmatic Hernia from Roentgenologic Viewpoint. B. R. Kirklin.—p. 642.

Wisconsin Medical Journal, Madison

48:665-772 (Aug.) 1949

Brain Tumors in Children. D. Cleveland.—p. 686.
Critical Evaluation of Sympathectomy in Peripheral Vascular Disease. M. DeBakey and A. Ochsner.—p. 689.
Aspects of Nutritional Anemias. J. B. Youmans.—p. 699.
Rheumatic Fever: Its Early Diagnosis. S. F. Morgan.—p. 704.
Penestration Operation: Selection of Cases and Training of the Surgeon. G. E. Shambaugh Jr.—p. 731.
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An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

Annals of Rheumatic Diseases, London

8:181-256 (Sept.) 1949

Subcutaneous Nodules of Rheumatoid Arthritis with Lipoid Deposition. M. Horwitz.—p. 181.
Can the Defence Mechanism of the Body be Influenced by Roentgen Irradiation? Report on Preliminary Clinical Investigation of Plasma or Serum Protein Pattern in Rheumatoid Arthritis. H. Ney.—p. 191.
Focal Infection in Rheumatoid Arthritis: Comparison of Incidence of Foci of Infections in Upper Respiratory Tract in 100 Cases of Rheumatoid Arthritis and 100 Controls. L. S. P. Davidson, J. J. R. Duthie and M. Sugar.—p. 205.
Plasma Viscosity. J. S. Lawrence.—p. 209.
Early Symptoms of Rheumatoid Arthritis. N. Egelius, N. G. Hivermark and E. Jonsson.—p. 217.
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Estimation of Gold in Biological Fluids. T. N. Fraser, H. Conway and S. L. Rae.—p. 223.
Salazopyrin in Treatment of Rheumatoid Arthritis. R. J. G. Sinclair and J. J. R. Duthie.—p. 226.
Value of Repeated Colloidal Gold Tests in Rheumatoid Arthritis. J. N. Swanson.—p. 232.

British Journal of Ophthalmology, London

33:461-524 (Aug.) 1949. Partial Index

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Final Results of Squint Operations, in Which Restoration of Binocular Single Vision Was Not Expected. A. Stanworth.—p. 477.
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Bilateral Symmetrical Tuberculous Ulcers of Bulbar Conjunctivae Treated with Streptomycin. B. K. Das Gupta and M. Usman. —p. 501.

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Preliminary Note on New Method of Fixing Corneal Grafts. C. A. Pittar.—p. 567.
Further Investigations on Action of Detergents on Eye. M. Ginsburg and J. M. Robson.—p. 574.
Artificially Produced Retinal Pulse. N. Pines.—p. 579.

British Medical Journal, London

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Use of Experience. H. Ogilvie.—p. 663.
Serological Classification of Viridans Streptococci from Subacute Bacterial Endocarditis, Teeth and Throats. P. R. Selbie, R. D. Simon and R. H. M. Robinson.—p. 667.
*Treatment of Early Syphilis with Penicillin Combined with Neoarsphenamine and Bismuth. J. W. Eames and D. H. Miller.—p. 672.
Sex Hormone Upset in Africans. J. N. P. Davies.—p. 676.
Direct Vein Graft in Rupture of Popliteal Artery: Report of Case. P. Martin.—p. 680.
Agglutinin Anti-M Associated with Pregnancy: Report on 2 Cases. C. C. Bowley and I. Donsford.—p. 681.
The Rhesus Factor D^u: Note on Its Practical Importance. F. Stratton and P. H. Renton.—p. 682.
Notes on Experimental Study of Intellectual Deterioration. S. Crown. —p. 684.

Treatment of Early Syphilis.—Eames and Miller describe the treatment of early syphilis employed by the Subcommittee on Venereology of the British Army. During an intitial period in hospital a course of 4,000,000 units of commercial penicillin (50,000 units in aqueous solution intramuscularly at three hour intervals for ten days) was given. On the second, fifth and ninth days the patient received an intravenous injection of neoarsphenamine, 0.3, 0.45 and 0.6 Gm., respectively, together with an intramuscular injection of 0.2 Gm. of a bismuth compound. On completion of this treatment and subject to his clinical condition, the patient was returned to military duty. Outpatient treatment, which was started seven days after his last injection of arsenic as an inpatient, consisted of eight weekly injections of 0.6 Gm. of neoarsphenamine and 0.2 Gm. of the bismuth preparation. Thus the total treatment was 4,000,000 units of penicillin, 6.15 Gm. of neoarsphenamine and 2.2 Gm. of the bismuth compound. It was possible to analyze the results of this treatment in 1,028 cases, which included 353 cases of seronegative and 443 cases of seropositive primary syphilis; the remaining 232 patients had early secondary syphilis. There was a high rate of "default" from surveillance due to the rapid release of patients from military service. If all patients who were considered to have become reinfected were considered to have relapses, then the total cumulative relapse rate at eighteen months was found to be 15 per cent and the cumulative mucocutaneous infectious relapse rate 8.2 per cent. If 4 of the 10 cases clinically diagnosed as reinfections are accepted as such, these relapse rates would be 10.8 and 5 per cent, respectively. These results would seem to be more satisfactory than those reported by others using commercial penicillin alone and in combination with oxophenarsine hydrochloride by the semi-intensive method. Treatment failures (cases showing seroresistance) were small in number, being 0.9 per cent of seropositive primary cases and 3.8 per cent of secondary cases. Toxic reactions occurred only in 3.51 per cent of all patients treated, and there were no fatalities.

Lancet, London

2:543-586 (Sept. 24) 1949

Clues to Aetiology of Graves' Disease. J. H. Means.—p. 543.
*Tuberculosis: Control of Infectious Disease. J. Francis.—p. 549.
Sequelae of Infective Hepatitis in Children: Review of 12 Cases. W. G. Wyllie and M. E. Edmunds.—p. 553.
Di-Isopropyl Fluorophosphonate as Intestinal Carminative. G. C. Arneil and A. S. Douglas.—p. 556.
Disseminated Sclerosis: Follow-Up of 91 Cases. J. H. D. Millar. —p. 556.
Experimental Typhoid Infection Treated with Chloromycetin and Sulphadiazine. A. W. El Borolossy and G. A. H. Buttle.—p. 559.
Perforated Enteric Ulcer Successfully Treated Conservatively. D. L. Stevenson and R. B. Welbourn.—p. 560.
Action of Soda Lime on Chloroform. H. L. Bassett.—p. 561.

Control of Tuberculosis.—Tuberculosis in cattle can be controlled over large areas when the tuberculin test is used and efforts are concentrated on breaking the chain of infection. Control of human tuberculosis is much more complex, because far less control can be exerted over human beings. Though chemotherapy may eventually come to play an important part, BCG vaccination is the one specific weapon that can now help to reduce the number of infected persons and the severity of new infections. Almost no work has been done in Great Britain on the standardization of the vaccine or methods of using it in man. There is abundant evidence that BCG increases resistance to tuberculosis in experimental animals, and this increased resistance is associated with the development of allergy. An allergic response is the criterion of successful BCG immunization, and there are good reasons for regarding allergy in immunized persons as direct practical proof of increased resistance. There seems to be no justification for withholding BCG vaccine from persons who want to use it or for exposing tuberculin-negative girls to tuberculous patients in order to obtain statistically satisfactory evidence of the value of BCG vaccination. The evidence supporting the use of BCG is already better than the evidence supporting any other immunologic procedure in man. The results of a number of controlled trials in the United States and in Scandinavian countries showed that BCG may cause a fivefold reduction in the morbidity and mortality of tuberculosis, which would be well worth achieving if only for the economy it would mean in surgical and sanatorium treatment. Human tuberculosis remains the most important single cause of death in Great Britain. What is required is not so much an "adequate trial" of BCG as a campaign which will begin a new "sanitary revolution" and control of the last of the great zymotic diseases in Great Britain.

Medical Journal of Australia, Sydney

2:265-300 (Aug. 20) 1949

Edward Stirling Lectures: I. Modern Trends in Surgery of Peptic Ulcer. K. W. Starr.—p. 265.
Series of Cases of Indirect Inguinal Hernia Treated by Method of Inversion of Sac. C. Craig.—p. 268.
Clinical Uses of Basal Body Temperature Graphs in Practice. A. Grant. —p. 271.
Review of Uses of Radioactive Iodine, with Note on Preliminary Work in Melbourne. R. K. Scott.—p. 273.
Treatment of Granular Proctitis with "Benadryl." T. E. Wilson. —p. 276.
Rubella Congenital Inner Ear Deafness in Tasmania. B. Hiller. —p. 277.
Results of Operative Treatment of Intervertebral Disk Protrusion: —p. 283.
Follow-Up Report of 108 Cases. D. Miller and G. K. Vanderfield.

Acta Chirurgica Scandinavica, Stockholm

98:221-604 (Sept. 3) 1949. Partial Index

Treatment of Cold Injury: Experimental Studies on Extremities of Rabbits. I. Effect of Periarterial Sympathectomy. S. Rönlén.—p. 268.
Papillomas of Choroid Plexus, with Report of Successfully Removed Tumour of Left Lateral Ventricle in 7 Months Old Child. G. Nerlén.—p. 273.
*Diagnosis of Intracerebral Hematomas Following Frontal Lobotomy. O. Sjöqvist, G. af Björkesten and U. Fernström.—p. 280.
Fractures of Cervical Spine in Children. G. Pettersson.—p. 288.
*Some Problems Concerning Herniated Intervertebral Disk from Clinical Point of View. S. Lindgren.—p. 295.
Internal Closure of Monaldi Fistula During Thoracoplasty with Extrapleural Apicolysis. J. Holst.—p. 315.
Reconstruction of Oesophagus. A. Ragnell.—p. 369.
Postoperative Emptying Difficulties in Direct Connection with Gastric Resection. E. Hjorth.—p. 385.
Carcinoids of Small Intestine and Stomach. S. O. Jonsson.—p. 390.
Surgical Treatment of Duodenal and Gastric Ulcers in Very Young Persons. T. Okovsca.—p. 396.
Treatment of Intestinal Gangrene in Infants. P. Sandblom and T. Ehrenpreis.—p. 404.
Surgical Treatment of Ulcerative Colitis. J. P. Strömbeck.—p. 414.
Radical Operations for Cancer of Rectum. A. Nielsen.—p. 428.
Some Observations on Removal of Kidney Stones Particularly by Means of Pyelolithotomy in Situ. J. Hellström.—p. 442.
*Renal Tuberculosis and Its Treatment by Partial Resection of Kidney. C. Semb.—p. 457.

Cerebral Hematomas Following Frontal Lobotomy.—Sjöqvist and his associates point out that Freeman and Watts recommended in 1942 injection of a few drops of iodized oil at the end of a frontal lobotomy in order to visualize the plane of section. In case the transection of the white matter should be incomplete the cut could be enlarged immediately. However, the drops of iodized oil may serve another purpose, namely, the early diagnosis of postoperative clots. A shift of the drops of iodized oil is probably the earliest sign of intracerebral oozing, thus enabling the diagnosis of an intracerebral hematoma even before clinical signs of intracranial expansion have appeared. In the Neurosurgical Department of the Södersjukhuset 99 frontal lobotomies were performed by the closed technic of Freeman and Watts between 1944 and 1948. Contrast medium, usually iodized oil, was introduced in 94 of the operations. Hypersensitivity of the patient to iodine had been ruled out by previous cutaneous tests. A few silver clips were applied at various levels in the patient in whom the preoperative test had demonstrated idiosyncrasy to iodine. Primary roentgenologic control in two planes was performed immediately after the operation in the 95 cases in which contrast medium had been introduced. In 1 case it was established that the incision had not been sufficiently deep. A second operation with deepening of the cut was immediately undertaken, with a more pronounced effect on the patient's symptoms. Renewed roentgenologic control one to two days after operation was carried out in 57 patients and revealed a considerable shift of the contrast medium in 4 patients. In one of these the clinical condition remained satisfactory. In the other 3 patients the presence of intracerebral hematomas was verified in second stage operations. No untoward effects of the iodine contrast medium have been observed. An unchanged position of the iodized oil twenty-four hours after the frontal lobotomy seems to indicate that postoperative oozing has not taken place.

Herniated Intervertebral Disk.—Lindgren reports 500 surgically verified cases of herniations of intervertebral disks, in all except 6 of which he was the surgeon. The typical case history of herniated intervertebral disk begins with lower back pain, which is an expression of the progressing degeneration of the disk and the formation of fissures in the annulus fibrosus. Gradually root symptoms supervene. Occasionally the history includes reports of attacks of sciatica. The dorsolumbar region often shows characteristic changes in the form of straightening and scoliosis. The normal lumbar lordosis may even be reversed to kyphosis. In nearly 60 per cent of the cases it is the disk between the lowest lumbar vertebra and the first sacral vertebra that is involved in the herniation, in nearly 40 per cent it is the disk between the fourth and fifth lumbar vertebrae, whereas the other lumbar disks are seldom involved. The neurologic root symptoms permitted exact localization of the involved disk in 75 per cent of the cases, whereas in the remaining 25 per cent more than 1 interstice had to be explored at operation. Myelography with contrast mediums should not be used as a routine method because of the irritating effects. Epileptiform attacks developed in 3 cases as the result of the use of contrast mediums. A myelogram interpreted as "normal" does not exclude a herniation. The author stresses the importance of a gentle operative technic and of painstaking hemostasis. There was usually a prompt disappearance of the symptoms after the operation, and nearly 90 per cent of the patients could be discharged from the hospital within three weeks. There may be complications and recurrences. Eighty-one per cent of the patients regarded the operation as decidedly beneficial and an additional 16 per cent as somewhat beneficial. In 70, or about 16 per cent, of the 500 cases, no herniation was found at operation although symptoms had suggested such a lesion. A follow-up disclosed that a majority of these had also benefited from decompression and a modified Albee procedure of root resection. Patients considering a disk operation can be assured that there is an 80 to 90 per cent chance of cure and no danger that the condition will be worse.

Renal Tuberculosis.—Semb feels that treatment of renal tuberculosis needs revision. The management of renal tuberculosis should be organized with pulmonary tuberculosis as a pattern. There must be efforts at early diagnosis, increased medical treatment and individualized selective surgical treatment. In the cases reviewed by the author treatment has been analogous with that for pulmonary tuberculosis. Medical and surgical treatment have been combined. Patients without evident destruction of tissue (shown by urography and pyelography) are treated medically. Those with local destructive lesions have been treated by local resection of the focus, those with total destruction by nephrectomy. The author has worked out a technic of partial resection of the kidney. This has been used in 14 instances, 5 of which involved bilateral disease. Sixteen resections and two nephrectomies have been performed. The mortality was nil. Postoperative urinary fistula, bleeding or spread of the disease has not been observed. At the end of treatment the 2 patients left with one half of one kidney are in good general health. It is too early to give an opinion on the final results as regards bacilluria. Of 6 patients observed more than nine months, 5 are free from urinary bacilli.

Deutsche medizinische Wochenschrift, Stuttgart

74:989-1036 (Aug. 26) 1949. Partial Index

Sympathetic and Parasympathetic Nerves. L. Seitz.—p. 989.
Therapeutic Problem of Acute Pancreatitis. E. Melchior.—p. 993.
*Two Years' Experiences with Urethane Therapy in Leukosis (1946-1948). II. Chronic Lymphadenosis (with Sarcomatosis of Lymphatic System). H. E. Bock and R. Gross.—p. 995.
Disorders of Water Metabolism in Diencephalopituitary Diseases and Their Diagnostic Significance. G. Damm.—p. 1008.

Urethane in Chronic Lymphadenosis.—Bock and Gross treated 15 patients having chronic lymphadenosis with ethyl urethane. The average total dose administered was 111 Gm. in thirty-two days. The required amount varied considerably with the individual patient from a minimum of 21 Gm. in seven days to a maximum of 219 Gm. in seventy days. Satisfactory results were obtained in 8 patients, partial success in 6, and failure in 1 patient. Excluding 1 case of the aleukemic type, the absolute number of cells was restored to nearly normal in 9 instances and reached half of the initial values in 4 instances. Urethane had little influence on the differential blood picture of chronic lymphadenosis. A slight increase in the lymphatic elements occurred in 4 instances; there was not much change in the percentage in 5 instances; a 20 to 30 per cent decrease occurred in 3, and a 30 to 50 per cent decrease in 2. The younger stages of the lymphatic series disappeared as a rule, but an increase in immature elements occurred once in the peripheral blood picture. The size of the lymph nodes was reduced in all but 2 instances. The size of the spleen remained unchanged in 4; the spleen was reduced to half its size in 3 instances, and in the other cases somewhat less, but it occasionally became softer.

A decisive decrease in leukocytes did not occur until two thirds of the required total dose of the drug had been given. "Phases of stimulation" in lymphocytopoiesis, i. e., more than 30 per cent increase in the number of the cells, occurred only in 3 instances, but without any change in the differential blood count. Nausea, vomiting, diarrhea, anorexia and sleeplessness occurred frequently, but these untoward reactions did not permit any conclusions as to the success of the treatment. The behavior of the hemoglobin represents an important criterion with respect to the value of the treatment. Considerable restriction of the spinal cord by lymphatic proliferation should not be considered as contraindication to urethane, provided the risk of myeloid insufficiency can be counteracted in time by the intramuscular administration of 30,000 units of penicillin every three hours and by blood transfusions. Considerable lymphatic proliferation, which does not subside completely after three courses of urethane, should be treated by roentgen irradiation. Temporary satisfactory results were obtained with ethyl urethane in 4 of 8 cases of sarcomatosis of the lymphatic system. There was a rapid and lasting decrease in the size of the lymph nodes, with reduction to normal for six months in 1 case. Such a remission may be considered as a satisfactory result of the urethane treatment in view of the generally unfavorable prognosis of lymphosarcomatosis. Roentgen irradiation should be instituted in cases in which the first course of urethane failed.

Gynaecologia, Basel

128:237-300 (Oct.) 1949. Partial Index

*Influence of Thyrotoxicosis on Menstruation. O. Riisfeldt.—p. 237.
Tubular Reabsorption of Chlorides in Eclampsia. D. Halmágyi and L. Zelenka.—p. 248.
Squamous Epithelium of Vaginal Type in Female Urethra. G. T. Hedberg.—p. 254.
New Considerations in Histologic Examinations of Endometrium in Connection with Sterility. L. Vaczy and E. Scipiades.—p. 260.

Influence of Thyrotoxicosis on Menstruation.—Riisfeldt of Copenhagen observed that of 309 sexually mature women with toxic diffuse goiter 95 had disturbances of the menstrual cycle. Fifty-one per cent had hypomenorrhea, 31 per cent had oligomenorrhea and 18 per cent had amenorrhea. The menstrual anomaly in 4 patients was the first subjective symptom of thyrotoxicosis. Regular menstruation was later reestablished in all except 6 of the patients who were reexamined. In 5 the examination had not been repeated. Patients over 30 years of age had menstrual anomalies somewhat more frequently than the rest. With a rising metabolic rate, an increasing number of patients had amenorrhea and hypomenorrhea. Of 8 patients with irregular menstruation before the onset of the thyrotoxicosis, 4 regained regular menstruation following their hyperthyroidism, and this condition persisted after operation.

Praxis, Bern

38:799-822 (Sept. 15) 1949. Partial Index

Bronchospirometry. E. P. Steinmann.—p. 799.
*Remarkable Activity of Proteolyzed Liver Extract in Pernicious Anemia. E. Martin and F. Vaucher.—p. 802.

Proteolyzed Liver Extract.—Martin and Vaucher report on a liver extract which has undergone proteolysis under the influence of the digestive ferment papain. This enzymatic action digests the proteins up to the polypeptide stage and makes it possible for the patient with pernicious anemia to utilize Castle's intrinsic factor. There is a solid and a liquid proteolyzed liver extract for oral use, as well as a highly concentrated proteolyzed extract for parenteral use. The authors used the latter in 15 patients with hyperchromic, macrocytic anemia. The injections caused little pain and have not given rise to allergic reactions. In patients in whom the diagnosis of pernicious anemia has been established, the authors inject 2 cc. of the extract per week. If a rapid effect is desired at the beginning, 4 cc. can be injected or 2 or 3 injections can be given with intervals of a few days. In the preparation of this injectable extract some of the B factors are destroyed to a considerable extent, but the vitamin B_{12} content remains high. The chief value of this extract is the fact that pernicious anemia can be effectively treated with it by four to eight injections per month. They were able to confirm the observations of British observers that this proteolyzed extract is 2 to 3 times more potent than ordinary whole liver extracts.

Revista Médica de Chile, Santiago

77:473-524 (Aug.) 1949. Partial Index

*Bronchogenic Carcinoma: Study of 40 Cases. H. Salvestrini, A. Lucchini and A. Marsano.—p. 480.

Bronchogenic Carcinoma.—Salvestrini and collaborators emphasize the importance of early diagnosis of bronchogenic carcinoma for segmental or lobar resection. They report observations on 40 patients between the ages of 20 and 70 with bronchogenic carcinoma, treated in the last two years in the Clinical Hospital of the Catholic University of Chile. Cough, expectoration, wheezing, hemoptysis, loss of weight, pain and in some cases fever were the early symptoms. The majority of the patients were in an advanced stage of the disease, at which the lumen of the bronchus was almost obstructed by the carcinomatous growth with consequent segmental or lobar infection. Diagnosis of bronchogenic cancer was made in 15 of 40 instances by roentgenography, in 8 of 26 by bronchoscopy, in 17 of 23 by cytologic study of the bronchial secretions and in 5 of 15 cases by an exploratory thoracotomy. Anteroposterior roentgenograms may conceal a segmental atelectasis which will show up in lateral roentgenograms. Roentgenograms showing local inflammation can disguise the growth or show changes indicating inoperability of the condition. Operability in cases of this nature should be decided by an exploratory thoracotomy, in the course of which segmental or lobar resection may be suggested by the biopsy.

Schweizerische medizinische Wochenschrift, Basel

79:817-848 (Sept. 10) 1949. Partial Index

Hemorrhagic Diatheses. R. Jürgens.—p. 817.
*Sporadic Hemophilia in Switzerland. A. Fonio.—p. 827.
Action on Hemophilic Plasma of Co-Factor of Thromboplastin Existing in Normal Plasma. R. Feissly.—p. 829.
Erythroblastic Splenomegaly and Myelosclerosis. H. Dubois-Ferrière and R. Della Santa.—p. 830.
Chronic Erythremic Myelosis with Positive Coombs Test. N. Quattrin. —p. 835.

Sporadic Hemophilia in Switzerland.—Fonio studied 24 families with instances of sporadic hemophilia. Among the families with a single sporadic hemophilic male there were 8 families with a tendency to hemorrhage in the conductor mother; in 2 instances the same tendency was reported in the grandmother and in 1 instance this tendency was suspected even in the great-grandmother, who died from uterine hemorrhage as the grandmother did. In 5 families with several hemophilic sons a tendency to hemorrhage was reported in the conductor mother as well as in the grandmother. In one of these families abnormally delayed clotting of the blood was demonstrated in 1 sister. The coagulation time was determined in 18 of the conductor women of the 24 families. An abnormally prolonged coagulation time could be demonstrated in 8 of the 18 women and a lowered coagulation time in 3. Mild and severe hemorrhages may occur in those with sporadic hemophilia. There may be periods with nearly complete absence of hemorrhages and periods with repeated hemorrhages. Prolonged times of coagulation of one to seven hours were demonstrated in 11 persons with sporadic hemophilia. The concept of sporadic hemophilia should be widened on the basis of the author's observations that several hemophiliac sons rather than only one hemophiliac male may occur in families which for generations did not have any hemophiliac members, and that in some of the conductor women the same tendency to hemorrhage may be demonstrated as in families with hereditary hemophilia. The tendency to hemorrhage in the conductor mother and in 3 instances in the grandmother does not make a primary sporadic hemophilia due to idiokinetic mutation of the hemophiliac son particularly likely but suggests a hemophiliac hereditary diathesis with latent transmission through several generations. The absence of the fully developed hemophiliac aspect of the disease may be explained by the covering of the X^1 chromosome by the healthy X chromosome, which may not be complete in the conductors with a tendency to hemorrhage.

Book Notices

THE REVIEWS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES AND DO NOT REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED.

Industrial Toxicology. By Lawrence T. Fairhall, Scientist Director, Public Health Service, Federal Security Agency, Chief, Industrial Hygiene Laboratory, Industrial Hygiene Division. Cloth. Price, $6. Pp. 483. Williams & Wilkins Company, Mt. Royal & Guilford Aves., Baltimore 2, 1949.

In his introduction Dr. Fairhall refers to this book as a manual and states that the material is based on the needs of the industrial hygienist and is as brief as is consistent with the hygienist's needs. The substances discussed are divided into two main groups—inorganic and carbon compounds. Each group is arranged alphabetically—something over 200 items. The characteristics of each substance are presented briefly. Then follows a short statement on industrial uses, toxicity and analysis and a short bibliography. The ten page index at the end is brief but usable. For instance, most substances are given by name only, like "plutonium," but one may find "ships, fumigation of," and "physiological response and chemical constitution." There is no author index or name index.

This book is easy to use, and subjects may be found quickly. It is startling to move along from nickel to nitrogen oxides to osmium, but one cannot miss the author's entries. There is a reasonable amount of cross indexing. The most interesting pages are in the introduction, where the author discusses chemical constitution and physiologic response and experimental toxicology. The author is particularly well qualified to discuss these subjects.

Rilievi anatomo-clinici sulle alterazioni vascolari in casi di malattia di Winiwarter-Buerger e di altre arteriopatie obliteranti croniche delle estremità. Dal Dott. Mario Austoni e Dott. Giorgio Candiani. Estratta da "Acta chirurgica patavina," Anno V, Vol. V, 1949, Fasc. 2. Paper. Pp. 102, with 17 illustrations. Scuola Tipografica Benedettina, Parma, 1949.

This monograph deals with a condition to which a variety of names has been applied, such as obliterating endarteritis, obliterating thromboangiitis, spontaneous juvenile gangrene, thromboangiosis, productive arteriophlebitis and Winiwarter-Buerger's disease. Various classifications of the disease are enumerated by the authors, who then proceed to the description of the clinical picture, differential diagnosis, etiology, pathogenesis and anatomic and histologic findings.

Four case histories of Buerger's disease, 3 of syphilitic arteritis, 6 of arteriosclerosis, 1 of typhoid arteritis and 2 of angiopathies attributable to a cervical rib are described in detail and are illustrated with photomicrographs. The authors conclude that two types of the disease can be differentiated: (1) Buerger's disease, which is obliterating endarteritis with an acute onset and tendency to migration and, (2) Winiwarter's disease, which is endangiitis involving the elastic-connective tissue and has a gradual onset and a chronic course.

The condition should be considered as a syndrome that can be provoked by a variety of infections or toxic agents. The concise treatise deserves attention of all interested in the pathogenesis of this disease.

Flebotrombosis y tromboflebitis de los miembros. Por Fernando Martorell. Con la colaboración de José Valls-Serra, et al. Ponencia en la primera reunión anual de la Sociedad española de cardiología. Paper. 36 pesetas. Pp. 130. Editorial Paz Montalvo, Madrid, 1949.

This essay is based on observations of 942 cases of venous thrombosis in 931 patients, 632 women and 299 men. The left extremity was affected twice as often as the right, while a bilateral lesion was found in 269 cases. The upper extremity was involved in only 22 instances. Of 931 patients, 140 developed pulmonary embolism. The interesting statistical data are followed by a thorough discussion of the evolution and the concept of thrombophlebitis. Separate chapters deal with the pathology, clinical manifestations, treatment and sequelae of the condition.

The book is well written, reviews the subject in compact form and has an exhaustive bibliography. It does not offer anything new for a specialist, but it forms a splendid guide to a graduate student.

Abraham Levinson Anniversary Volume: Studies in Pediatrics and Medical History in Honor of Dr. Abraham Levinson on His Sixtieth Birthday. Dr. Solomon R. Kagan, Editor. Editorial Board: Dr. Isaac A. Abt, Dr. Reuben Friedman, Prof. Max Neuburger. Cloth. $6. Pp. 365, with illustrations. Proben Press, Inc., 1776 Broadway, New York 19, 1949.

This book, dedicated to Dr. Abraham Levinson, Chicago pediatrician, is a tribute from friends and admirers here and abroad. It contains original contributions from medical men of international renown. The volume is divided into four sections. The first is devoted to pediatric neurology and psychiatry, Dr. Levinson's special field of endeavor. Of particular interest in this group are the papers on midline intracranial tumors in the posterior fossa of children by Loyal Davis, John Martin and Daniel Ruge and on parental attitudes as pathogenic agents by Leo Kanner.

The second section of the book deals with blood and cerebrospinal fluid, a field in which Dr. Levinson has done pioneer work. Especially noteworthy in this section are the articles by Samuel Amberg and G. B. Logan on thermal destruction of blood catalase; by I. Davidsohn, K. Stern and C. Kashiwagi on infectious mononucleosis; by Reuben Kahn on precipitation studies on cerebrospinal fluid, and by A. S. Wiener on the rhesus (Rh) factor of human blood.

The third portion of the book is concerned with general pediatrics. Here one finds such interesting papers as S. van Creveld's on chronic renal disease and osteoporosis, Ludwig Meyer, N. Bogair and I. Heyman on purulent meningitis due to an unidentified pleomorphic bacillus; Arthur Parmelee's on hormonal inadequacies in the premature infant, and Hans Popper and Bruno Volk on hepatitis with jaundice in children.

The fourth section is on medical history. A particularly illuminating article is the one by Arturo Castiglioni of Italy on the history of medicine, with special reference to the medical historian, Abraham Levinson. Other interesting papers are those by Morris Fishbein on Paracelsus, Reuben Friedman on Bonomo and Cestoni, Max Neuburger on Stephen Hales and Bela Schick on geographic differences in disease.

At the end of the book, there is an extensive bibliography of Dr. Levinson's books, chapters and articles with annotations by the editor. The book is well illustrated and clearly printed.

The book is a treasure house of the recent advances in pediatrics and the significant events in medical history. It should prove of great value to pediatricians, neurologists and research workers and would be a fine addition to a medical library.

De prognose van de initiele longtuberculose. Door George Antonius Gussenhoven. [Prognosis of Initial Stages of Pulmonary Tuberculosis.] Proefschrift ter verkrijging van de graad van doctor in de geneeskunde aan de Rijksuniversiteit te Leiden. Paper. Pp. 152, with illustrations. N. V. Wed. J. Ahrend en Zoon, Amsterdam, 1949.

This thesis discusses the prognosis of early minimal tuberculosis of the reinfection type and is based on material collected in the tuberculosis dispensary at the Hague. After the short historical introduction, the various theories on the development of initial pulmonary tuberculosis are presented. Of these, the subclavicular origin of the "early infiltrate," which has never met the approval of the pathologists, is considered most important. In 1938, the roentgen observations of Malmros and Hedvall indicated the initial foci were found in the cranial aspects of the lungs with no preference shown for the subclavicular regions. These are miliary pneumonias, recognized by the pathologists as initial phthisis a long time ago. A description of the objective and subjective symptoms of these foci is given. In the second chapter the author discusses the therapy of these lesions and conservative management is advocated. A chronologic survey of the literature indicates that the prognosis of these foci is a questionable one. In the third chapter the author notes 379 patients during 1924 to and including 1938. These presented lesions which, on the basis of roentgenographic and clinical symptoms, might be regarded as early minimal tuberculosis of the reinfection type. The proportion of men to women was 2 to 3, and the average age was 24 years. After a 13 year period of observation, 99 (26 per cent) had died, 23 (6 per cent) were still suffering from tuberculosis, 257 (68 per cent) had recovered, 236 (62 per cent) were treated in a sanatorium, 59 (16 per cent) had bedrest at home and 64 (22 per cent) had no

treatment at all. All the aforementioned groups showed about the same mortality rate. Twenty-six patients (7 per cent) did not respond to any therapy. Forty-four patients (12 per cent) recovered spontaneously. About half the number of patients had a relapse. With prolonged treatment, relapses were fewer and there was a lower mortality rate. In the fourth chapter statistics are discussed and methods of research of the factors influencing prognosis are described. In the fifth chapter the factors are evaluated with the following results: 1. The prognosis is not influenced by the lesions being right or left, lesions being cranialward, history of family tuberculosis, contact, sex, age, combination of history of family tuberculosis with age or contact and the combination of sex and age. 2. The prognosis is unfavorably influenced by high sedimentation rate, positive sputum, bilateral lesions, incipiency of lesion, short treatment, unfavorable proportion of length and weight of the patient and by the large lesions. 3. Favorable conditions are a normal sedimentation rate, negative sputum, presence of symptoms, prolonged treatment, favorable proportion of length and weight and the small lesions.

This monograph appears to have made some practical deductions on the basis of prolonged observations and which can well be heeded in the future control of the tuberculous patient. Much of it is not particularly new, but its crystallization gives added confidence for future guidance. It is in Dutch, but the book is short and may be worthy of complete translation.

*** Neuere Tuberkulosoforschung 1: Verhandlungsbericht des ersten Kongresses der wissenschaftlichen Gesellschaft süddeutscher Tuberkulosefürsorgeärzte 25.-27. September 1948 auf dem Rohnhorn bei Oberstdorf Allgäu.** Erstattet von Obermedizinalrat Dr. Griesbach, Tuberkulose-Bücherei, Monographien zur Monatsschrift "Der Tuberkulosearzt." herausgegeben von Dr. Rolf Griesbach und Dr. Otto Wiese. Paper. Price, $2. Pp. 112. [Grune & Stratton, 381 4th Ave., New York 16]; Georg Thieme, Diemershaldenstrasse 47, Stuttgart-O, 1949.

This monograph contains 18 reports presented before the South German Tuberculosis Society, including tuberculosis of domestic animals, industrial significance of bovine tuberculosis, bovine tuberculosis in man, statistics evaluation, control of open tuberculosis, nontuberculous complications in the treatment of pulmonary tuberculosis, new differential diagnosis of inflammatory processes in the thorax, chemotherapy of tuberculosis, streptomycin treatment of tuberculous meningitis, pathologic-anatomic aspects of chemotherapy, operative treatment of pulmonary tuberculosis, pulmonary tuberculosis and interruption of pregnancy and bioclimatic treatment and methods. The desire for exchange of ideas in 1948 resulted in this scientific society of South German Tuberculosis Physicians, and, in spite of handicaps, this is the report of the first congress. The variegated nature of the brief reports on the many phases of tuberculosis makes it impossible for a reviewer to give more than a few casual remarks. The volume is adapted only to those who can read German fluently. The subjects pertain primarily in the statistical and economic parts to the south German areas and are thus limited. Though brief, the subjects are handled ably in a postgraduate refresher manner, and the discussions are elucidating, though more in abstract form. A favorable report of the use of Domagk's T B 698 for the treatment of intestinal tuberculosis claims a more rapid resolution, equaling the action of streptomycin and a para-aminosalicylic acid at less cost. Collapse procedures are reviewed in all aspects. Weather (and climate) changes are physiologic, and the reaction in disease depends on the individual irritability of the vegetative system as well as the presence of pathologically changed tissues. It is concluded that further chemical and meteorologic studies are desirable as well as artificial methods. Future reports of the scientific congress are anticipated.

Étude sémiologique de tonus musculaire. Par André Thomas et J. de Ajuriaguerra. Paper. 2000 francs. Pp. 944. Éditions Médicales Flammarion, 22, Rue de Vaugirard, Paris, 6e, 1949.

This excellent volume deals with all the types of pathologic tonus states of the striated muscles of man. The first section (90 pages) deals with methods of examination of muscle tonus pathology, with clear and useful illustrations. It is a useful book for all doctors with an adequate knowledge of French.

Clinical Studies of Besnier's Prurigo: Synonyms: Atopic Dermatitis, Eczema Prurigineum Allergicum, Neurodermatitis Disseminata, with Special Reference to its Course, the Significance of Airborne Allergens and the Value of Certain Methods of Treatment. By P. H. Nexmand. Denne afhandling er af det lægevidenskabelige Fakultet ved Københavns Universitet antaget til offentlig at forsvares for den medicinske Doktorgrad, 1948. Paper. Pp. 236, with 31 illustrations. Rosenkilde & Bagger, Copenhagen, 1948.

This monograph reviews the literature and the author's studies of this baffling disease, variously labeled atopic dermatitis or disseminate neurodermatitis. In a series of 100 patients, the author observed that the disease has a seasonal fluctuation, improves with a change of environment, is questionably improved with some forms of desensitization and treatment with ultraviolet rays, and is not cured by antihistaminic drugs. The reader is left with the feeling, unfortunately often true, that the most beneficial therapeutic influence in this disease is change of environment. The author believes that this change is helpful from the standpoint of altered or minimal allergen exposure. Other factors of equal or even greater importance, such as psychosomatic interplay, are not afforded adequate consideration in this clinical study.

Die doppelseitige Nierenkrankheiten Morbus Brightii: Eine Neurolpathologische Betrachtung. Von Prof. Dr. Wilhelm Nonnenbruch. Half-cloth. Price 21.20 marks. Pp. 210, with 15 illustrations. Ferdinand Enke, Hasenbergsteige 3, Stuttgart, W, 1949.

Nonnenbruch describes the anatomy, physiology and pathology of the kidneys and blood vessels. Emphasis is placed on the role of the nervous system in their regulation rather than on the kidneys and heart. Chapters on arterial hypertension, nephritis and nephrosis, their etiology, clinical course and treatment, complete the book.

Since Professor Nonnenbruch occupies a position of authority in Europe, his book assumes rather more than usual interest and importance. With certain outstanding exceptions, he probably reflects current teaching in Germany and some allied countries.

The book is readable and succinct. The typography is good, and the book is cheaply bound. The literature available to Nonnenbruch is almost wholly German; consequently, there is little or no mention of the work pursued in this country and England on modern methods of examination, such as of the kidneys, renal or cerebral blood flow and mechanisms of hypertension. The thinking is that of twenty years ago, which merely reflects the tragedy and results of war. The book can be recommended only as a reflection of the knowledge of a group of thoroughly capable clinicians whose development was blocked by the intellectual desert of war, from which recovery has not even yet occurred.

Lawson Tait 1845-1899. By I. Harvey Flack, M.D. Cloth. Price, 17s.6d. Pp. 148, with 13 illustrations. William Heinemann, Ltd., 99 Great Russell St., London, W.C.1, 1949.

The place of Lawson Tait in the history of gynecology has been a matter of dispute. To most of his contemporaries, he was a surgical swashbuckler whose wholesale "spaying" of women was a blot on the honor of the profession. Moreover, no less a medical historian than Fielding Garrison dismissed him as "a forcible, effective, frequently coarse, not entirely truthful, but always amusing writer." On the other hand, William J. Mayo called him "the father of modern abdominal surgery" and Joseph Price said: "In pelvic surgery Tait stood first and taught us the best we know."

This small volume, published on the fiftieth anniversary of Tait's death, sets forth the factual evidence on both sides of the question, and the reader may draw his own conclusions. That Tait was on the wrong side of many issues cannot be denied, and his wrathful outbursts against Listerism and animal experimentation, as well as his high-handed denunciation of his contemporaries, are no credit to him. As Flack points out, however, this ruthlessness in debate as well as at the operating table was a necessary weapon to force on an apathetic profession the merits of pelvic surgery. Thus, his greatest contributions, namely, the operative treatment of ruptured ectopic pregnancy and of pus tubes, were the objects of almost universal condemnation and only a fortitude which was callous to criticism could have carried through the fight.

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After documenting both sides of the question, Flack's conclusion would seem to be inevitable, namely, despite his avowed shortcomings, Tait did more than any other person to create a gynecologic specialty and to blaze the trail for the great generation of abdominal surgeons that followed. To gynecologists who have found McKay's lengthy work on Tait unduly exhaustive, this succinct biography can be warmly recommended as an absorbing as well as authoritative account of one of the most colorful figures in all medicine.

Chirurgia d'urgenza. Da Stefano Tonoff. Cloth. 5500 lire. Pp. 1024, with 482 illustrations. Edizioni Minerva medica, Via Martiri della Libertà, 15, Torino, [1949].

The progressive evolution of the treatment of surgical emergencies made a revision of such classical works as Lejars' book imperative. The author has undertaken the tremendous task of covering the entire field and accomplished it in an admirable manner.

The book is divided into two parts. The first deals with the general principles of first aid. The author describes in a succinct manner the proper preparation of the patient and the surgeon, sedation, choice of anesthetics, selection of incision and treatment of hemorrhage and shock. He discusses first aid for traumatic lesions of blood vessels, nerves, muscles and tendons, bones and articulations and surgical infections.

The second part offers an outline of treatment of emergencies, according to topography of the lesion. First aid in fractures is described in a long chapter. Injuries of the eyes, ears, the oral cavity and the genitourinary apparatus have not been omitted.

A cursory review failed to disclose any mention of absorbable sponges. The apparatus for venoclysis and for blood transfusions appear outmoded according to American standards.

The author has achieved a remarkably thorough coverage of the subject. The volume is profusely illustrated by photographs, roentgengrams and schematic drawings. The effective use of one other color, such as red, yellow or blue, in addition to black, adds to the instructive value of the illustrations. The book is accurate and contains an adequate index.

This manual forms a splendid guide to first aid and should have a special appeal to residents and industrial surgeons.

Cirugía de la glándula tiroides: Anatomía quirúrgica del cuello al nivel hueso hioideo superior y su relación con la fisiología hueso, los aponeurosis cervicales, con un apéndice sobre tiroidectomía. Por Diego H. Zavaleta. Prólogo del Profesor Ricardo Finochietto. Cloth. $40.-m/n. Pp. 154, with 38 illustrations by C. A. Vescovo. Ediciones Impagliano, Venezuela 1702, Buenos Aires, 1949.

Twenty-eight dissections of cadavers form the basis of this volume on surgical anatomy of the thyroid gland, with special attention to aponeurotic and fascial sheaths and the topography of the superior laryngeal nerves. A short discourse on physiology of the larynx precedes the chapters on surgical anatomy. They are followed by a short chapter on physiopathology, devoted to the description of the sequelae of lesions of the superior laryngeal nerve or its branches. A chapter on the surgical technic closes the book, which is profusely illustrated with photographs of the dissected specimens and with schematic drawings, many in color.

The author is focusing his attention nearly exclusively on the topographic relations of the superior laryngeal nerve. Although in no sense sufficiently comprehensive to serve as an atlas of surgical anatomy of the thyroid gland, the volume is a splendid contribution to the subject and should be of great value to those interested in goiter surgery.

Diagnostik durch Sehen und Tasten: Eine Synthese der Inspektion und Palpation. Von H. Kahler. Paper. Price, 2.70. Pp. 233, with 10 illustrations. Springer-Verlag, Möllerbastei 5, Vienna 1, 1949.

The author of this book is one of the oldest surviving students of the famous Chvostek, to whose memory this work is appropriately dedicated. It marshalls an extraordinary number of facts and suggestions showing how inspection and palpation can contribute to diagnosis. The book is written in a commendably simple, compact and objective style that should give little trouble to a reader reasonably versed in scientific German. Space and time are saved by stating conflicting opinions with few comments but copious references; the bibliography is excellent. The book will be an inspiration to medical students and may serve to correct the present tendency to rely too much on laboratory data. The author regrets the loss of much illustrative material during the war, and it is hoped that future editions may be better illustrated.

It is also to be hoped that a future edition will see the elimination of those vicious words "Degenerationszeichen" and "Abartungszeichen" (stigmas of degeneracy) from the book; the index actually contains more than two columns of entries under the latter caption. It is deplorable to see these terms applied to insignificant variations ranging from pigmented moles to supernumerary nipples. The late Hugh Patrick did humanity a service by protesting against the continued use of these sinister-looking yet scientifically meaningless words in medical literature, for the amount of psychic trauma their use has inflicted on persons already handicapped has been incalculable. In every other respect this book can be recommended heartily, especially to students of physical diagnosis.

Essentials of Orthopaedics. By Philip Wiles, M.S., F.R.C.S., F.A.C.S., Consulting Orthopaedic Surgeon, Royal Surrey County Hospital, Surrey, England. Cloth. Price $10. Pp. 486, with 272 illustrations. The Blakiston Company, Division of Doubleday & Company, Inc., 1012 Walnut St., Philadelphia 5; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W.1, 1949.

The contents of this book reflect the author's extensive experience in the field of orthopedics. The essential subjects are covered in a standard manner but are presented from the author's point of view. The material is selected and represents the generally accepted current conceptions. No space is given to historical development, and there is no chapter on fractures.

The first two chapters are concerned with postural defects and back pain, which are encountered with greatest frequency in clinical orthopedic practice. In the chapter on postural defects and back pain, considerable importance is attached to the position of the hip and the condition of hip musculature in the causation and treatment of these two conditions. The author accepts weakness in the small rotators of the spine to be the most logical causative basis for idiopathic scoliosis. Considerable space is allotted to various changes in the intervertebral disk. The main portion of the book is divided into separate chapters, each dealing with a separate portion of the body. The various orthopedic conditions are discussed as they are encountered in each region. Certain aspects of orthopedics which involve the entire body are included in separate chapters. These general subjects include pyogenic infections, tuberculosis, chronic arthritis, bone tumors, diseases of the nervous system and generalized congenital defects and diseases of bone. In general, the book is well arranged, well written and adequately illustrated.

La Streptomycine et le "PAS" dans le traitement de la tuberculose chez l'enfant. Par Max-Henri, Béguin, médecin-assistant à l'Hôpital Jenner, Berne. Bibliotheca paediatrica, Supplementa zu Annalen paediatrici, Jahrbuch für Kinderheilkunde. Fasc. 49. Redactor: H. Freudenberg. Paper. 5 Swiss francs. Pp. 96, with 14 illustrations. S. Karger, Holbeinstrasse 22, Basel; 215 4th Ave., New York 3, 1949.

This small pamphlet describes the results obtained at the Jenner Hospital, Berne, Switzerland, with the use of streptomycin and para-aminosalicylic acid in the treatment of tuberculosis in infants and children. Considerable space is devoted to reviewing the literature, and the remainder is devoted to detailed case histories of children with various types of tuberculosis. In general, the response to streptomycin therapy observed by the author in children parallels that observed by others in adults. Too few cases of tuberculosis treated with combinations of streptomycin and para-aminosalicylic acid are reported to permit the author to make more than tentative conclusions. He believes, however, that the concurrent use of para-aminosalicylic acid in tuberculous meningitis permits reduction in dosage of streptomycin, particularly if it is to be given intrathecally, to a level which will rarely produce the distressing toxicity often associated with vigorous treatment of this form of tuberculosis.

This volume has little new information to offer, but the experience of the author with regard to dosage in infants and children and the toxic effects of the two drugs may be of interest to those engaged primarily in the treatment of tuberculosis.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

PERIODICALLY PAINFUL BREASTS

To the Editor:—Please suggest treatment for bilateral mastodynia in a 33 year old patient. At times the pain occurs just before her menstrual period, associated with a typical premenstrual tension syndrome. At other times pain lasts throughout the month. The breasts are large, but there are no obvious masses. Large doses of vitamin B complex and ammonium chloride, 4 Gm. daily, give some transient relief. Would methyl testosterone be worth while?

M.D., Pennsylvania.

[Ed. Note—The opinions expressed in the following answers by consultants indicate that no one treatment of this condition is always effective.]

ANSWER.—Endocrine therapy has been disappointing in providing continued relief for painful breasts. Several authors have suggested the use of androgens in the latter half of the cycle. However, although they may alleviate some of the discomfort, their long-continued use may lead to some undesirable concomitant masculinizing effects.

Painful breasts in young women are best treated by adequate support. A properly fitted brassiere which will gently pull the breasts upward and inward, without undue pressure on them, will alleviate much of the discomfort.

ANSWER.—Painful swelling of the breasts preceding menstruation can often be relieved by the administration of estrogen alone or by the administration of estrogen followed by progesterone. If estrogen is given alone, it should be administered for three weeks following the cessation of each menstrual period. If it is combined with progesterone, the progesterone should be started before the onset of the next period.

Methyl testosterone will help, but it is unwise to use androgen therapy in women unless it is absolutely necessary, because of the danger of inducing masculinizing changes.

ANSWER.—Treatment should include an adequate dosage of thyroid extract, based on the metabolic rate, 3 drops of Lugol's solution daily, and 4 grains of whole pituitary extract orally three times daily; 1 cc. of whole pituitary solution with an additional 5 mm. of posterior pituitary solution intramuscularly twice each week for one month, and ammonium chloride 0.5 Gm. three times a day every second week, alternating with 5 grains of potassium chloride given three times a day. Sodium in the diet should be reduced. Many patients respond to the administration of 10 cc. of 10 per cent solution of calcium levulinate intravenously twice weekly every second month for six months. In addition estrogenic substances (water soluble), 1.25 mg., should be given orally every third day for three doses beginning on the fourth day of menses. If the patient does not respond after two months, 1.25 mg. should be given orally three times daily for twenty days following menstruation and on the tenth day progesterone should be added (10 mg. three times a day for ten days). As soon as menstruation begins again repeat treatment with estrogenic substances and progesterone, using two doses daily. In the third month repeat the medication, using one dose of each daily.

Good results have been reported from administration of diethylstibestrol, 0.5 mg. daily during the second and third weeks following menstruation. Methyl testosterone is contraindicated in these conditions.

HAIR DYE

To the Editor:—Is paraphenylenediamine, which is used in making hair dye, injurious to the scalp if used for a number of years? The patient in question does not appear to be allergic to it.

Alice E. Moore, M.D., New York.

ANSWER.—A statement by the Federal Food and Drug Administration concerning paraphenylenediamine type of hair dye indicates that of every 1,000 persons who use it, 15 will be found sensitive to the first application, 25 will acquire sensitivity with continued use of the dye and 960 will be unaffected. There is little, if any, danger of permanent injury to the scalp. Aside from cases of dermatitis, there have been few reported cases of unfavorable reactions involving the eyes and central nervous system.

X-RAY MACHINES

To the Editor:—1. Can 15 or 20 milliampere machines be used for roentgenograms of the chest at a distance of 6 feet (183 cm.)? Do machines with only slightly higher rating (e. g., 60 milliamperes) have any advantages? 2. If one had only a fluoroscope, would it be practical with training to screen patients by observing the passage of barium through the stomach and pylorus and to determine which ones should be referred to the roentgenologist for further study? Would one be exposing his patient to too much irradiation? Would early detection of cancer be possible? 3. At 3 to 5 milliampere settings on an ordinary vertical fluoroscope, how many seconds or minutes of exposure is within safe limits for fluoroscopic examination of the chest?

S. Richard Horio, M.D., Honolulu, Hawaii.

ANSWER.—1. Satisfactory roentgenograms of the chest cannot be obtained with a 15 or 20 milliampere machine at a distance of 6 feet. However, it is doubtful whether this distance is necessary for your work; 4 feet (122 cm.) probably would be sufficient. The smaller machine would be fairly efficient for the latter distance, although a standard bedside unit of 30 milliampere capacity would be preferable.

2. Roentgenoscopic examination of the kind contemplated may reveal occasionally an early cancer or other small lesion, but consistent exhibition of such lesions is not easy even for the well trained radiologist. Nevertheless, the general practitioner should not be discouraged from making such examinations, he may find disease that would otherwise escape discovery. He should bear in mind, however, that failure to observe evidence of cancer may give patient and physician an unjustified sense of security. If there are symptoms indicative of cancer or other organic disease of the stomach or bowel, he should send the patient to a capable radiologist for examination. If roentgenologic examination is to be relied on to detect or exclude early cancer, it must be repeated at least every three months.

3. Roughly, two to five minutes would be the extreme limit. The examiner should be cautioned concerning his own safety, if he examines many patients, for the lungs absorb few of the rays and fluoroscopic examination of the chest is more hazardous than fluoroscopic examination of the stomach and bowel.

CONGENITAL DEAFNESS

To the Editor:—The condition of my son, aged 17 months, has been diagnosed as congenital deafness. The otolaryngologist says that there is no sign of an infectious process. A negative history of any ear infection and another case of congenital deafness in a distant relative were the basis for the diagnosis. What is the present status of therapy for this condition? Beginning two days after birth and lasting for about three months, projectile vomiting, diagnosed as pyloric spasm on a gastrointestinal series, was present, relieved greatly by belladonna. Could this have been a factor in the production of deafness? Is it advisable to start such a child to kindergarten in special school? Can the names of several special schools for the deaf be supplied? Although this is a first baby, labor was rapid (two hours), necessitating a rapid and deep induction of anesthesia. The infant was delayed in breathing, which was attributed to aspiration of amniotic fluid, and a tracheal catheter was used in resuscitation. Subsequently an incubator was used for a day. Could this have played a part in the production of deafness? Physical examination reveals no defect except the probable loss of hearing.

M.D., Tennessee.

ANSWER.—There is no effective medical or surgical treatment for congenital deafness. It is unlikely that the vomiting during the first three months of life was a factor in this deafness, as there has been no report in the literature about deafness following protracted vomiting. A child this age should be started on an integrated home training program. For information, consult the John Tracy Clinic in Los Angeles or the Volta Bureau in Washington. It is doubtful whether it would be advisable to place the child in school at this age. As much as possible, deaf children should be kept in a normal home environment. The following are schools for the deaf: Central Institute for the Deaf, St. Louis; Clarke School for the Deaf, Northampton, Mass.; Wright Oral School, New York, and Lexington Avenue School for the Deaf, New York.

Prolonged anoxia can produce cerebral deterioration. However, it has not been shown that the neuromechanism of hearing is more susceptible than other portions of the central nervous system. Inasmuch as the child seems to have normal maturation in other respects, it is doubtful whether anoxia was a factor. Auditory aphasia is seen on rare occasions, but its presence cannot be readily demonstrated at this age.

If the hearing loss were due to blocked eustachian tubes, the drums would show changes, and the hearing loss in all probability would not be severe. Radiation therapy is not indicated on the basis of the present observations.

MACERATED FETUS

To the *Editor*:—A married woman aged 29 delivered normally a female child in 1943. In 1930 she had a major abdominal operation for a cyst of the hepatic duct. She has had no trouble related to the upper part of her abdomen since. In 1945 she had a major operation. The present pregnancy began early in 1948, her last regular menstrual period being January 23. Reaction of the blood to the Wassermann test was negative; she was Rh positive, and she seemed to be normal throughout pregnancy. She had a mild amount of nausea and vomiting. Her expected date of delivery was estimated as October 30. In September examination revealed the baby to be in a breech position and external version was done without any difficulty. On October 26 she went into labor and delivered without any difficulty in a few hours. The fetus was stillborn and macerated, and on questioning the patient stated that she had last felt fetal movement twenty-four hours before the onset of labor. Recombination of the patient's blood showed it to be Rh positive, and checking against the husband's blood there is no homolymph reaction at all. I have been at a loss to explain this occurrence.

David L. MacDonell, M.D., Sayville, N. Y.

ANSWER.—It is difficult to reconcile the fact that the fetus was macerated with the patient's statement that she had last felt fetal movement twenty-four hours before the onset of labor, particularly when the bag of waters ruptured just before labor began and delivery took place in a few hours. Slight maceration can occur within twenty-four hours after death, but presumably the maceration was fairly extensive. If the latter is true, and certainly if the fetus was small, one must consider that fetal death possibly followed the external version performed a month before delivery. The patient could have been mistaken about the presence of fetal movements after the version. Of course, if the heart tones were heard a few days or more after the version, the latter procedure could not have been responsible for the fetal death. Nothing was said about the presence or absence of fetal heart tones either during or immediately after the external version. Nor is there any mention of bleeding after the version or the presence or absence of blood clots on the placenta. Occasionally there is separation of the placenta during external version and this has caused the death of the fetus.

ANTIHISTAMINE THERAPY

To the *Editor*:—Is it possible that antihistamine therapy as now proposed by many pharmaceutic houses might be a factor in lowering the resistance to pollens? In other words, if the administration of antihistamine drugs is stopped, is it possible that the patient might be more sensitive?

Thomas S. Fleming, M.D., Moberly, Mo.

ANSWER.—The present antihistamine compounds produce their effect in the allergic reaction by competitive replacement of some of the histamine attaching itself to cells after its liberation as a result of the antigen-antibody (allergic) reaction. Certain experiments indicate that some of these compounds might also have other action beneficial to allergy, such as diminishing capillary permeability and vasoconstrictor action. All experimental evidence, both in anaphylactic hypersensitivity in animals and in allergy in man, indicates that these compounds do not interfere with the antigen-antibody reaction, the production of antibodies (such as precipitins or blocking antibodies in man) or clinical desensitization. The antihistamine compounds possess many undesirable features, but they cannot be accused of interfering with the process of desensitization. The intemperate use of antihistamine drugs in place of desensitization, has caused considerable damage in creating a false sense of security, since they cannot take the place of desensitization, especially when asthma is part of the syndrome.

ADENOMA OF THYROID GLAND

To the *Editor*:—In what percentage of persons having adenoma of the thyroid gland may carcinoma and sarcoma of that gland develop, and how long would it take such a condition to supervene from the time the adenoma was first observed?

F. L. Milligan, M.D., Santa Monica, Calif.

ANSWER.—Most investigators agree that when malignant degeneration in the thyroid gland occurs it is commonly in adenomas and rarely in diffuse toxic goiter. The percentage incidence of this change varies somewhat with reports from different geographic areas and with the criteria used by pathologists.

The incidence of malignancy in adenomatous goiter, including those with multiple and solitary nodules, has been reported by Horn and his co-workers to be 5.5 per cent, by Ward 4.8 per cent and by Cole and his co-workers 7.2 per cent. In a study made at the University of Michigan it was 6.94 per cent. Hinton and Lord reported an incidence of 7.6 in a series of cases seen on the Atlantic seaboard. These figures are based on surgically removed glands and represent a higher figure than would be found by routine autopsy examinations.

In an analysis of sixty-one cancers, there were fifty-six that were epithelial in origin and therefore carcinomas, and five were identified as sarcomas, an incidence of 91.8 and 8.2 per cent, respectively. Conclusive facts are not available concerning the length of time an adenomatous goiter must exist before malignant degeneration occurs. A nodular goiter, either of multiple or solitary type, seen in a patient of any age, should be regarded as a precancerous lesion. If changes in size have recently been noted, the lesion should be regarded as probably malignant and treated by immediate operation.

CYANHIDROSIS

To the *Editor*:—Kindly discuss the diagnosis and treatment for a patient who perspires blue sweat. This 35 year old plastic salesman has had a thorough examination and laboratory studies. Only an allergic diathesis and possibly spastic colon could be found. Careful questioning has not revealed any source for the blueness of the perspiration. It is not due to clothing.

M.D., New Jersey.

ANSWER.—Genuine idiopathic cyanhidrosis is rare. Infrequently, in the presence of intestinal tract putrefaction, an excessive amount of indol is formed. This in turn becomes indoxyl and indican, which may appear in sweat as blue indicanhidrosis. Tests for indican should be made on the urine; some indican (about 12 mg.) is normally present in the twenty-four hour specimen. Usually, there is only a mild blue tinting of the sweat that is limited to a few areas, such as around eyes, cheeks, axillas and groins. If it is more widely distributed, an effort should be made to collect a few cubic centimeters of sweat, on which indican tests can be carried out. The skin should be cleansed of all blue discoloration, and with a hand lens, an examination made of the skin orifices. If they are not blue, the subsequent blueness is due to the action of Bacillus pyocyaneus or other bacterium or fungi or to some surface chemical. The sweat may be cultivated for detection of blue-forming organisms. Furthermore, intake of some iron or copper substances rarely may induce cyanhidrosis, although copper more often produces greenish sweat discoloration. Even copper in dental prostheses may cause color in the sweat. The possibility of deception should not be overlooked.

FERTILITY OF BINOVULAR TWINS

To the *Editor*:—Are there any studies on the relative fertility of binovular twins? In a rather large family, the only two not able to have children are a pair of binovular twins (male and female) aged 47.

M.D., Wyoming.

ANSWER.—The idea that twins are likely to be infertile probably derives from the fact that the so-called freemartin, female twin to a bull calf, is usually sterile. In such cases the placentas fuse; testicular secretion from the male fetus then finds its way into the blood of the female and inhibits the development of her reproductive organs.

No such sequence of events has been observed in human beings, nor is there any other known special mechanism which would tend to cause sterility in a human twin of either sex. Though statistics are not available, the impression is that both single ovum and double ovum twins are on the average as fertile as other persons.

Since one marriage in eight or nine is involuntarily childless, the laws of chance could easily explain the occurrence of two such matings in any large family group. The fact that in the present instance each of the two sterile matings involves a twin is probably no more than a coincidence. Adequate diagnostic study would doubtless reveal obvious factors of infertility in both couples.

DIABETES INSIPIDUS AND MARRIAGE

To the *Editor*:—A 28 year old woman has had diabetes insipidus since she was 18. She has been taking posterior pituitary by nasal insufflation. The patient is getting married and would like to know whether this condition is to be expected in her children and whether the insufflation is likely to interfere with pregnancy.

Fritz Koenig, M.D., Catlin, Ill.

ANSWER.—Diabetes insipidus is an inheritable condition, and there are various reports in the literature regarding the occurrence of the disease in one or more generations of a family. Most cases, however, appear to occur at random. In the

patient described, if there is not a history of diabetes insipidus in relatives, the chances are good that the condition would not appear in her child.

The insufflation of posterior pituitary intranasally will in sufficient dosage cause contractions of the uterus. Consequently, during pregnancy its use, as well as the surgical and obstetric use of posterior pituitary by injection, should be undertaken cautiously. However, beta-hypophamine is stated not to contain the oxytocic principle in significant amounts and so should be better tolerated. A suitable preparation for long-continued action would appear to be beta-hypophamine tannate in oil given intramuscularly (Blotner, H., and Kunkel, P.: Diabetes Insipidus and Pregnancy, *New England J. Med.* **277**: 287 [Aug. 20] 1942; Blotner, H.: The Inheritance of Diabetes Insipidus, *Am. J. M. Sc.* **204**: 261 [Aug.] 1942).

DIET AND INSULIN IN DIABETES

To the Editor:—At a meeting of an association for former interns, I asserted that the proper management of diabetes is by control of diet, with insulin used only to supplement the diet except in emergencies, in which insulin would have to be used to bring a patient out of coma or for rapid preparation for major surgical treatment. I was surprised to learn that two professors of medicine disagreed with this program, contending that the treatment of diabetes was with insulin, the diet being used as a secondary measure. What is the prevailing point of view, my concept or that of the two professors?

M.D., New Jersey.

Answer.—Most clinicians experienced in the treatment of diabetes regard restriction of diet as fundamental in treatment. Although some have advocated a "free diet," the experience of most physicians has led them to believe that patients do better both in the immediate present and the distant future by following a carefully regulated diet. Such a diet should be adequate in protein, minerals and vitamins and should furnish sufficient calories to maintain normal weight and strength. Restriction must be most careful as regards carbohydrate, and many physicians use with success diets for adult patients which provide 150 to 200 Gm. of carbohydrate a day. Fat is adjusted according to the body weight and caloric needs of the patient. Obesity is a handicap to the diabetic patient, and it is common that with loss in weight the obese adult diabetic patient shows improvement in his carbohydrate tolerance.

If, on a diet which is necessary to maintain weight and strength, a diabetic patient is not aglycosuric or nearly so and has blood sugar values which are not within a satisfactory range, then insulin should be used without hesitation. Methods vary considerably, but in certain clinics in which large groups of diabetic patients are treated as high as 80 per cent receive insulin. Although in other clinics the percentage of insulin-treated patients is lower, the general aims and principles of treatment remain the same.

CARCINOMA OF THE CECUM

To the Editor:—A woman aged 38 had adenocarcinoma of the cecum. The growth was removed with adequate resection of the cecum. Four lymph glands were excised, and only two were found to be involved. Will testosterone propionate 50 mg. three times weekly be of any value in this case?

M.D., California.

Answer.—No record can be found of the use of androgens in the treatment of adenocarcinoma of the cecum. The use of androgens in the treatment of cancer of the breast is being thoroughly studied (J. A. M. A. **140**: 1193 and 1214, Aug. 13, 1949). On the basis of knowledge accumulated in these studies, a response of tumors in which endocrine factors do not appear to play a significant role would not be expected. On the other hand, it is possible that in the presence of bone metastases, regardless of the location of the primary tumor, some relief of pain might be noted due to the metabolic effects of testosterone, particularly the actions on calcium and phosphorus metabolism. Since the case described does not have bone metastases, there is apparently no sound indication for androgen therapy, particularly if any other recognized form of treatment has not been adequately explored.

IONTOPHORESIS IN ARTHRITIS

To the Editor:—Where may I obtain information on the use of iontophoresis in arthritis? Please name one or more manufacturers of this equipment.

Louis J. Polskin, M.D., Lakeland, Fla.

Answer.—A critical discussion of the clinical use of iontophoresis, or ion transfer (preferred term), is given by Stafford L. Osborne in the "Handbook of Physical Medicine" (Chicago, American Medical Association, 1945, pp. 193-198). A briefer statement will be found in "Apparatus Accepted" for Jan. 1, 1949, copies of which can be had free of charge from the Council on Physical Medicine and Rehabilitation. The Council publication lists five manufacturers of direct current generators that can be used for this purpose.

DISTURBANCES AFTER PREFRONTAL LOBOTOMY

To the Editor:—Should there be any interference with the centers which regulate the body temperature after prefrontal lobotomy? I have noticed in some cases that fever occurs more easily and is severer than in normal persons. The elevations of temperature occur with exposure to the sun as well as in illness.

B. R. Baker, M.D., Staunton, Va.

Answer.—Disturbances in the vegetative apparatus are common after prefrontal lobotomy, particularly in the early post-operative phases. This applies to pulse rate, blood pressure and respiration more than it does to body temperature. The vegetative imbalance is more pronounced in cases where the incisions trespass on the posterior half of the base of the frontal lobe. Patients who show decided febrile reactions to exposure and to infection are usually rather inert, indicating that a radical operation has been performed. The lack of complaints by these patients is often the reason why the temperature rises to unaccustomed heights before the febrile state is recognized.

FECAL IMPACTION

To the Editor:—I saw a patient 80 years of age with a severe fecal impaction. The roentgenogram of the colon was negative except for a "markedly atonic and dilated colon." This patient is constipated and must be given an enema every three days to prevent recurrence of the impaction. She does not tolerate ordinary cathartics. I read in the June 11, 1949 issue of THE JOURNAL (p. 522) of the use of urecholine® (urethane of beta-methylcholine chloride) in adynamic ileus and was wondering whether this drug might benefit this patient.

M.D., Illinois.

Answer.—Urethane of beta-methylcholine chloride if given in adequate doses may produce some peristaltic activity of the colon; however, abdominal cramping and pain also may be anticipated. Its use is not recommended for constipation. In general the use of any strong cathartic or drug to force hard stool through the distal colon is unwise. It is assumed that a tumor of the rectum or rectosigmoid, not infrequently missed by roentgen examination, has been ruled out by sigmoidoscopy. Suggest a regular diet including fruits and vegetables. There is no objection to the occasional administration of small tap water or oil enemas if the stool is hard and fails to pass the rectum.

HEREDITARY DEAFNESS AND MUTISM

To the Editor:—In Queries and Minor Notes in The Journal July 2, 1949, page 849, the reply on hereditary deafness and mutism states that "it may be due to an intrauterine cochlear damage from quinine, also transmitted through the placenta." I was shocked by this opinion, which I thought was a thing of the past. Only 17 cases of congenital deafness or visual disturbances in children whose mothers took quinine during pregnancy were recorded in medical literature between 1933 and 1948, all in American publications. Since then no cases were recorded; no cases of this kind have ever been mentioned in British, French, German, Spanish or Dutch literature. I published a paper (Quinine and Congenital Injuries of Ear and Eye of the Foetus, *J. Trop. Med.* **51**: 2, 1948) refuting the opinion that quinine was the causative agent in hereditary deafness. I pointed out that: (a) according to the census of 1930 deaf-mutism and congenital blindness do not occur more frequently in malaria districts of the United States (where great quantities of quinine used to be consumed) than in noncorresponding regions; (b) the world consumption of quinine used to be 600,000 to 800,000 Kg. a year, which quantity would have produced many more cases of deaf-mutism and blindness, if quinine really endangers fetal organs, than have actually been recorded, and (c) it should not be forgotten that these cases were all published before there was any suspicion of the deleterious influence of rubella of the mother on her fetus.

C. W. F. Winckel, M.D.,
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Amsterdam, The Netherlands.

DRYNESS OF SKIN

To the Editor:—In the *Journal*, Oct. 1, 1949, page 362, under the heading "Dryness of the Skin," there appears the statement "If the basal metabolic rate is low, therapy with thyroid substance is indicated. . . ." I wish to call attention to the fact that the basal metabolic rate is not a good index of whether thyroid extract should or should not be used. It is well known that thyroid extract is often most effective when the basal metabolic rate is above 0 per cent. The basal rate determination is therefore misleading as a therapeutic guide. Better criteria are a good evaluation of the clinical picture, blood cholesterol, galactose tolerance curve (especially in hypothyroid states) and blood iodine and, in children, roentgenograms of the bones.

William Weil, M.D., New York.